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<input type="checkbox"/>	L8	(L7 and TAA)	9
<input type="checkbox"/>	L7	(L6 and (dendritic adj cell))	57
<input type="checkbox"/>	L6	(L4 and (APC or dc))	67
<input type="checkbox"/>	L5	(L4 and (cancer adj grade))	1
<input type="checkbox"/>	L4	(L3 and (fusion adj protein))	85
<input type="checkbox"/>	L3	(L2 and prostate)	115
<input type="checkbox"/>	L2	(L1 and (prostatic acid phosphatase))	136
<input type="checkbox"/>	L1	(pap and (gm adj csf) and cancer)	996

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#24	Search prostatic acid phosphatase and GM-CSF	12:41:55	9
#23	Search pap and (gm-csf) and adrenal	12:41:20	0
#22	Search pap and (gm-csf) and pancreas	12:41:12	0
#21	Search pap and (gm-csf) and ovary	12:41:06	0
#20	Search pap and (gm-csf) and stomach	12:41:00	0
#19	Search pap and (gm-csf) and rectum	12:40:53	0
#18	Search pap and (gm-csf) and colon	12:40:47	0
#17	Search pap and (gm-csf) and larynx	12:40:40	0
#15	Search pap and (gm-csf) and breast	12:39:49	2
#14	Search pap and (gm-csf) and bladder	12:39:37	0
#13	Search pap and (gm-csf) and endometrium	12:39:28	0
#11	Search pap and (gm-csf) and lung	12:39:02	47
#12	Search pap and (gm-csf) and lung and phosphatase	12:38:53	0
#10	Search pap and (gm-csf) and bone	12:37:37	8
#9	Search pap and (gm-csf) and cervix	12:37:30	0
#8	Search pap and (gm-csf) and uterine	12:37:23	0
#7	Search pap and (gm-csf) and esophagus	12:37:12	0
#6	Search pap and (gm-csf) and brain	12:36:49	1
#4	Search pap and (gm-csf) and lymphoma	12:35:59	2
#3	Search pap and (gm-csf) and sarcoma	12:35:14	1
#2	Search pap and (gm-csf) and prostate	12:34:42	7
#1	Search pap and (gm-csf) and prostate	12:34:35	6

Clear History

Jun 14 2006 10:29:54

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NEWS 6 FEB 22 Updates in EPFULL; IPC 8 enhancements added
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second quarter; strategies may be affected
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NEWS 18 MAY 19 Derwent World Patents Index to be reloaded and enhanced
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NEWS 21 JUN 02 The first reclassification of IPC codes now complete in
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=> s (pap and gm (w) csf) and cancer)
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number of left parentheses.

=> s (pap and (gm (w) csf) and cancer)
L1 31 (PAP AND (GM (W) CSF) AND CANCER)

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L3 17 (L2 AND PROSTATE)

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L4 17 DUPLICATE REMOVE L3 (0 DUPLICATES REMOVED)

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L1 31 S (PAP AND (GM (W) CSF) AND CANCER)
L2 25 DUPLICATE REMOVE L1 (6 DUPLICATES REMOVED)
L3 17 S (L2 AND PROSTATE)
L4 17 DUPLICATE REMOVE L3 (0 DUPLICATES REMOVED)

=> d l4 bib abs 1-17

L4 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:1321617 CAPLUS
TI Safety and immunological efficacy of a prostate cancer
plasmid DNA vaccine encoding prostatic acid phosphatase (PAP)

AU Johnson, Laura E.; Frye, Thomas P.; Arnot, Alana R.; Marquette, Carrie;
Couture, Larry A.; Gendron-Fitzpatrick, Annette; McNeel, Douglas G.
CS Department of Medicine, Section of Medical Oncology, K4/518 Clinical
Science Center, University of Wisconsin-Madison, Madison, WI, 53792, USA
SO Vaccine (2006), 24(3), 293-303
CODEN: VACCDE; ISSN: 0264-410X
PB Elsevier B.V.
DT Journal
LA English
AB Prostatic acid phosphatase (PAP) is a **prostate** tumor antigen currently being investigated as a target antigen in several human vaccine trials, some with evidence of clin. benefit. We have previously demonstrated that plasmid DNA vaccines encoding either human or rat PAP can elicit antigen-specific cellular and humoral immunity in rat models. The current study was performed to determine the safety and potential immunol. efficacy in rodents of large and repetitive doses of a GMP-grade plasmid DNA vaccine encoding human PAP, pTVG-HP. Fifty-four male Lewis rats were immunized intradermally at 2-wk intervals with 100, 500, or 1500 µg pTVG-HP with 5 µg recombinant rat GM-CSF protein given as a vaccine adjuvant. An addnl. 12 male Lewis rats served as controls with groups immunized with 1500 µg of a parental DNA vector not encoding human PAP, and a group that received GM-CSF protein only without plasmid DNA. Groups of animals (n = 3-6) were euthanized after two, four, or six immunizations with collections of tissues and blood for toxicity assessment and immunol. anal. No significant toxicities were observed in terms of animal wts., histopathol., hematol. changes, or changes in serum chemistries. Six of fifty-four were found to have subtle evidence of possible renal toxicity, however these findings were not statistically different from control animals. The vaccine was found to be effective in eliciting PAP-specific CD4 and CD8 T cells, predominantly Th1 in type, in all immunized animals at all doses and nos. of immunizations. PAP-specific IgG were detected in a dose-dependent fashion, with titers increasing after multiple immunizations. These studies demonstrate that, in rats, immunization with the pTVG-HP vaccine is safe and effective in eliciting PAP-specific cellular and humoral immune responses. These findings support the further clin. evaluation of pTVG-HP in patients with **prostate cancer**.

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:72938 CAPLUS
TI Provenge: **prostate cancer** therapy
AU McIntyre, J. A.; Fernandez, D.
CS Prous Science, Barcelona, 08080, Spain
SO Drugs of the Future (2005), 30(9), 892-895
CODEN: DRFUD4; ISSN: 0377-8282
PB Prous Science
DT Journal; General Review
LA English
AB A review. There are few therapeutic options available for the treatment of hormone-refractory **prostate cancer** (HRPC), but recent advancements in the understanding of immune recognition have resulted in the development of novel vaccine products aimed at inducing **prostate**-specific T-cell-mediated immunity. Provenge (APC-8015) is an immunotherapeutic consisting of autologous dendritic cell precursors loaded ex vivo with a recombinant fusion protein (PA2024) comprising prostatic acid phosphatase (PAP), an antigen found in 95% of **prostate cancers**, and granulocyte-macrophage colony-stimulating factor (GM-CSF). Early clin. studies demonstrated good tolerability of the product and T-cell proliferation responses to PA2024. Phase II studies indicated the preliminary efficacy of Provenge, with increases in **prostate**

-specific antigen (PSA) doubling time and PSA-modulating effects.
Subsequent placebo-controlled phase III studies identified advantages for Provenge in terms of time to disease progression and time to onset of disease-related pain.

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:1127402 CAPLUS

DN 142:54751

TI Alternative reading frame peptides as antigens for the prophylaxis and treatment of **cancer** and infectious diseases

IN Graddis, Thomas; Laus, Reiner; Diegel, Michael; Vidovic, Damis

PA Dendreon Corporation, USA

SO PCT Int. Appl., 147 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004111075	A2	20041223	WO 2004-US6979	20040305
	WO 2004111075	C1	20050519		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	CA 2514288	AA	20041223	CA 2004-2514288	20040305
	US 2005112134	A1	20050526	US 2004-794514	20040305
	EP 1601684	A2	20051207	EP 2004-749357	20040305
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK			
PRAI	US 2003-453131P	P	20030305		
	WO 2004-US6979	W	20040305		
AB	Alternative reading frame (ARF) peptides associated with disease conditions and that can be recognized by antigen presenting cells (APC) and dendritic cells (DC) are described for use as antigens in the diagnosis, treatment, and prevention of diseases including cancer and infectious diseases. These peptides may arise from frameshifting, use of alternative start codons, ribosomal skipping, suppression of termination of translation, translation of antisense transcripts, splice variants or use of cryptic promoters. Alternative reading frame peptides derived from the HER-2 receptor gene were incubated with mouse dendritic cells in vitro and the cells reintroduced into the donor mice. Mice challenged with B16 cells blocked tumor growth, whereas animals treated with inframe HER-2 proteins did not.				

L4 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:287861 CAPLUS

DN 140:320038

TI Chimeric and humanized anti-granulocyte antibodies, immunoconjugates and labeled antibodies for diagnosis and treatment of malignancy, infection and inflammation

IN Goldenberg, David M.; Hansen, Hans; Leung, Shui-on

PA Immunomedics, Inc., USA; McCall, John Douglas

SO PCT Int. Appl., 134 pp.

CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004029093	A2	20040408	WO 2003-GB4229	20030930
	WO 2004029093	A3	20040603		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	CN 1542019	A	20041103	CN 2003-123054	20030429
	CA 2500250	AA	20040408	CA 2003-2500250	20030930
	AU 2003269225	A1	20040419	AU 2003-269225	20030930
	EP 1546204	A2	20050629	EP 2003-751001	20030930
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			

PRAI US 2002-414341P P 20020930
WO 2003-GB4229 W 20030930

AB The present invention provides humanized, chimeric and human MN3 antibodies, fusion proteins, and fragments that bind NCA90 and NCA95 antigens. The antibodies, fusion proteins, and fragments thereof, as well as combinations with other suitable antibodies, are useful for the treatment and diagnosis of granulocyte related disorders and diseases, such as leukemia.

L4 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:270002 CAPLUS

DN 140:302326

TI Immunotherapeutic compositions comprising antigen presenting cells (APCs) stimulated by fusion proteins (such as APC binding protein fused to tumor-associated antigen), and use of compositions in treatment of moderately to well-differentiated **cancers**

IN Laus, Reiner; Gold, Mitchell; Madhusudan, Peshwa; Pickering, Grant; Kylstra, Jelle; Peshwa, Madhusudan

PA Dendreon Corporation, USA

SO PCT Int. Appl., 66 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004026238	A2	20040401	WO 2003-US29176	20030919
	WO 2004026238	C1	20040722		
	WO 2004026238	A3	20041209		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	CA 2497554	AA	20040401	CA 2003-2497554	20030919
	AU 2003267254	A1	20040408	AU 2003-267254	20030919

US 2004161413	A1	20040819	US 2003-666122	20030919
EP 1540627	A2	20050615	EP 2003-749725	20030919

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRAI	US 2002-412271P	P	20020920
	US 2003-475355P	P	20030602
	US 2003-475335P	P	20030602
	WO 2003-US29176	W	20030919

AB The invention discloses immunotherapeutic compns. comprising activated antigen presenting cells (APCs), wherein said APCs were obtained from **cancer** patients and stimulated by exposure ex vivo to a fusion protein composed of a APC binding protein and tumor-associated (specific) antigen. The invention also discloses the use of said stimulated/activated APCs in treatment of patients with moderately to well-differentiated **cancer** cells. The invention further provides a method of assessing in **cancer** patients the susceptibility of **cancer** to said immunotherapeutic compns. As way of illustration, the invention discloses a fusion protein (APC8015) composed of a portion of **prostate** tumor-associated protein human prostatic acid phosphatase (huPAP) at the N-terminus and a portion of APC/DC binding protein human granulocyte-macrophage colony stimulating factor (huGM-CSF) at the C-terminus. APC stimulated by exposure ex vivo to said **PAP/GM-CSF** fusion protein were effective in activating T cells to produce a cytotoxic cellular response against huPAP. Finally, the invention discloses the amino acid sequences of huPAP and huGM-CSF. In the examples, the invention demonstrated that the therapeutic efficacy of immunotherapeutic compns. comprising APCs stimulated with **PAP/GM-CSF** fusion protein correlates with the differentiation state of the **prostate cancer** cells. Specifically, it was demonstrated that patients exhibiting moderately to well-differentiated prostate **cancer** cells were susceptible to treatment with said immunotherapeutic composition. The invention also demonstrated the efficacy of a combined immunotherapeutic treatment regimen that includes administration of **PAP/GM-CSF**-pulsed dendritic cells in conjunction with administration of humanized anti-VEGF monoclonal antibody Bevacizumab in patients having a serol. progression of **prostate cancer**.

L4 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:589231 CAPLUS
DN 141:134058
TI Methods and compositions for treating **prostate cancer** using DNA vaccines
IN McNeel, Douglas
PA Wisconsin Alumni Research Foundation, USA
SO U.S. Pat. Appl. Publ., 39 pp.
CODEN: USXXCO

DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	---	-----	-----	-----
PI	US 2004142890	A1	20040722	US 2003-669474	20030925
PRAI	US 2002-413777P	P	20020927		

AB A DNA vaccine for the treatment of **prostate cancer**, comprising a plasmid vector comprising a nucleotide sequence encoding prostatic acid phosphatase (**PAP**) operably linked to a transcription regulatory element, wherein upon administration to a mammal a cytotoxic immune reaction against cells expressing **PAP** is induced. In preferred embodiment, the **PAP** encoded is a xenoantigen highly homologous to the autoantigen **PAP** of the mammal. Also disclosed are methods for inducing prostatitis, or inducing immune reaction to **PAP**, or treating **prostate**

cancer in a mammal, using the DNA vaccine and pharmaceutical compns. comprising the vaccine. Preferably, xenoantigen vaccination is followed by boosting with autoantigen **PAP** from the same animal species as the mammal being treated. Lewis rats immunized with pTVG-HP, encoding human **PAP**, developed **PAP**-specific cellular immunity and **prostate** tissue inflammation.

L4 ANSWER 7 OF 17 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2004-21964 BIOTECHDS

TI Treating **cancer** with an immunotherapeutic composition comprises determining differentiation state of **cancer** cells, where presence of moderately to well-differentiated cells indicates patient susceptible to treatment with the composition;
composition for **cancer** immunotherapy comprises dendrite cell exposed to tumor-associated antigen

AU LAUS R; GOLD M H; PESHA M; PICKERING G; KYLSTRA J
PA DENDREON CORP

PI US 2004161413 19 Aug 2004

AI US 2003-666122 19 Sep 2003

PRAI US 2003-666122 19 Sep 2003; US 2002-412271 20 Sep 2002

DT Patent

LA English

OS WPI: 2004-614827 [59]

AN 2004-21964 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - Treating (M1) a **cancer** patient with an immunotherapeutic composition where the patient has a **cancer** with moderately to well-differentiated **cancer** cells, comprising determining the differentiation state of the **cancer** cells, where the presence of moderately to well-differentiated **cancer** cells indicates a patient susceptible to treatment with an immunotherapeutic composition, and administering the composition, where a reduction of 10% indicates an effective treatment of the **cancer**, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an immunotherapeutic composition (I) comprising activated, isolated antigen presenting cells (APCs) that are obtained from a patient diagnosed with a **cancer** having a moderate to well-differentiated **cancer** grade and are stimulated by exposure ex vivo to a tumor-associated antigen (TAA); (2) inhibiting (M2) growth of a **cancer** cell in a patient having a moderate to well differentiated **cancer** grade, comprising determining the differentiation state of the **cancer** cells, where the presence of moderately to well-differentiated **cancer** cells indicates a patient susceptible to treatment, isolating APCs from the patient, stimulating the APCs by exposure ex vivo to the immunotherapeutic composition comprising a protein conjugate having an N-terminal moiety and a C-terminal moiety, where the APCs are effective to activate T-cells to produce a cytotoxic cellular response against either the N-terminal moiety or the C-terminal moiety and where the level of the T-cell activation is higher than that produced by the APCs when exposed exclusively to the N- or C-terminal moiety, and administering to the patient the stimulated APCs, where a reduction of 10% indicates an effective treatment of the **cancer** and (3) a method of assessing in a **cancer** patient the susceptibility of the **cancer** to an immunotherapeutic composition, comprising isolating from the patient a sample containing the **cancer** cell, and determining the differentiation state of the **cancer** cell, where a moderate to well differentiated **cancer** grade indicates that the **cancer** is susceptible to treatment with an immunotherapeutic composition.

WIDER DISCLOSURE - Also disclosed are nucleic acids, polypeptides, host cells, vectors and antibodies used in the methods of the invention.

BIOTECHNOLOGY - Preferred Method: The composition is (I). Preferred

Composition: The TAA of the immunotherapeutic composition is a tumor-specific antigen, or is a component of a protein conjugate comprising an N- and C-terminal moiety. The APCs are dendritic cells. The **cancer** is soft tissue sarcomas, lymphomas, and **cancers** of the brain, esophagus, uterine, cervix, bone, lung, endometrium, bladder, breast, larynx, colon/rectum, stomach, ovary, pancreas, adrenal gland or **prostate**. The **cancer** grade corresponds to a Gleason score of at most 7. The patient is not refractory to hormone ablation therapy. The N- or C-terminal moiety is an APC binding protein an/or a TAA. The fusion protein further comprises, between the N- and the C-terminal moiety, a linker peptide. The N- or C-terminal comprises a sequence having at least 70, 80, 90 or 100% identical to huPAP or huGM-CSF with a fully defined sequence of 386 or 144 amino acids (SEQ ID NO: 1 and 3), respectively, as given in the specification.

ACTIVITY - Cytostatic; Immunostimulant. Prior to initiating an immunotherapeutic treatment regimen with PAP/GM-CSF fusion protein (APC8015) or placebo, patients were assessed for baseline disease characteristics. To determine the differentiation state of **prostate cancer** cells, **prostate** tissue samples were isolated from each patient and subjected to analysis by the Gleason scoring methodology as described in Gleason, Urologic Pathology: The **Prostate**, pp. 171-197 (Tappenhau, ed., Lee and Fehiger, Philadelphia, Pa., 1977). Time to objective disease progression was defined as progression on bone scan or x-ray or clinical deterioration and the data were subjected to statistical analysis by the Kaplan-Meier methodology. PSA was not used to determine disease progression. The median time to disease progression for the patient population treated with APC8015 was 11.0 weeks whereas the median time to disease progression for the patient population treated with placebo was 9.1 weeks. The data demonstrated that patients having poorly differentiated **prostate cancer** cells were refractory to treatment with APC8015 as evidenced by the absence of a statistically significant difference (p-value=0.431) in time to objective disease progression for the patient population treated with APC8015 as compared to the patient population treated with the placebo. In contrast, the results obtained for patients exhibiting moderately to well-differentiated **prostate cancer** cells (having a Gleason score of less than or equal to 7) show that such patients were susceptible to treatment with an immunotherapeutic composition as evidenced by the high degree of statistical significance (p-value=0.002) in time to objective disease progression for the patient population treated with APC8015 as compared to the patient population treated with the placebo.

MECHANISM OF ACTION - None given.

USE - For treating **cancers** including soft tissue sarcomas, lymphomas, and **cancers** of the brain, esophagus, uterine, cervix, bone, lung, endometrium, bladder, breast, larynx, colon/rectum, stomach, ovary, pancreas, adrenal gland or **prostate** (claimed).

ADMINISTRATION - Routes of administration of the pharmaceutical compositions include oral, pulmonary, intramuscular, intraperitoneal, intravenous, subcutaneous, inhalation, transdermal, nasal, vaginal, rectal and sublingual. No dosages given.

ADVANTAGE - The method is based upon the observation that the grade of a **cancer** cell, being a measure of the cell's differentiation state, is predictive of clinical outcome in **cancer** patients undergoing an immunotherapeutic treatment regimen. Whereas poorly differentiated cells were found to be refractory to an immunotherapeutic treatment regimen, moderately to well-differentiated cells were highly susceptible to treatment with immunotherapeutic compositions. (34 pages)

induce durable remission of metastatic androgen-independent

prostate cancer: a phase 2 trial

AU Burch, Patrick A.; Croghan, Gary A.; Gastineau, Dennis A.; Jones, Lori A.;
Kaur, Judith S.; Kylstra, Jelle W.; Richardson, Ronald L.; Valone, Frank
H.; Vuk-Pavlovic, Stanimir

CS Division of Medical Oncology, Department of Oncology, Mayo Clinic,
Rochester, MN, USA

SO Prostate (New York, NY, United States) (2004), 60(3), 197-204

CODEN: PRSTDS; ISSN: 0270-4137

PB Wiley-Liss, Inc.

DT Journal

LA English

AB **Prostate cancer** is the most commonly diagnosed malignancy in American men, yet treatment of its metastatic androgen-independent form remains inadequate. This mandates development of new therapies such as immunotherapy. In this Phase 2 trial, we determined the efficacy of antigen presenting cells (APCs) loaded with PA2024, a recombinant fusion protein containing prostatic acid phosphatase (PAP) and GM-CSF. We enrolled 21 patients with histol. documented androgen-independent **prostate carcinoma** that could be evaluated by radionuclide bone scan or computed tomog. scan. APC8015 was prepared from a leukapheresis product; it contained autologous CD54-pos. PA2024-loaded APCs with admixts. of monocytes, macrophages, B and T cells. APC8015 was infused i.v. twice, 2 wk apart. Two weeks after the second infusion, patients received three s.c. injections of 1.0 mg of PA2024 1 mo apart. We monitored patients' phys. condition, immune response, and laboratory parameters. Nineteen patients could be evaluated for response to treatment. The median time to progression was 118 days. Treatment was tolerated reasonably well; most adverse effects were secondary to APC8015 and were NCI Common Toxicity Criteria Grade 1-2. Four of the 21 patients reported Grade 3-4 adverse events. Two patients exhibited a transient 25-50% decrease in **prostate-specific antigen (PSA)**. For a third patient, PSA dropped from 221 ng/mL at baseline to undetectable levels by week 24 and has remained so for more than 4 yr. In addition, this patient's metastatic retroperitoneal and pelvic adenopathy has resolved. PBMC collected from patients for at least 16 wk proliferated upon in vitro stimulation by PA2024. For the patient with responsive disease, PBMC could be stimulated for 96 wk. This study demonstrates a definite clin. response of androgen-independent **prostate cancer** to APC immunotherapy. Currently we are studying this mode of therapy in Phase 3 trials.

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2003:719518 CAPLUS

DN 139:259962

TI Humanized murine anti-epithelial glycoprotein 1 (EGP-1) antibodies RS7 and
conjugates for diagnosis and treatment of **cancer**

IN Govindan, Serengulam; Qu, Zhengxing; Hansen, Hans J.; Goldenberg, David M.

PA Immunomedics, Inc., USA; McCall, John Douglas

SO PCT Int. Appl., 97 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003074566	A2	20030912	WO 2003-GB885	20030303
	WO 2003074566	A3	20040304		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,			

PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
 UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2478047	AA	20030912	CA 2003-2478047	20030303
AU 2003209447	A1	20030916	AU 2003-209447	20030303
US 2004001825	A1	20040101	US 2003-377121	20030303
EP 1483295	A2	20041208	EP 2003-743420	20030303

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

CN 1649903	A	20050803	CN 2003-809918	20030303
JP 2006502698	T2	20060126	JP 2003-573031	20030303

PRAI US 2002-360229P	P	20020301
WO 2003-GB885	W	20030303

AB This invention relates to monovalent and multivalent, monospecific binding proteins and to multivalent, multispecific binding proteins. One embodiment of these binding proteins has one or more binding sites where each binding site binds with a target antigen or an epitope on a target antigen. Another embodiment of these binding proteins has two or more binding sites where each binding site has affinity towards different epitopes on a target antigen or has affinity towards either a target antigen or a hapten. The present invention further relates to recombinant vectors useful for the expression of these functional binding proteins in a host. More specifically, the present invention relates to the tumor-associated antigen binding protein designated RS7, and other EGP-1 binding-proteins. The invention further relates to humanized, human and chimeric RS7 antigen binding proteins, and the use of such binding proteins in diagnosis and therapy.

L4 ANSWER 10 OF 17 BIOTECHNO COPYRIGHT 2006 Elsevier Science B.V. on STN

AN 2003:37239077 BIOTECHNO

TI Cell therapy and **prostate cancer**

THERAPIE CELLULAIRE ET **CANCER DE LA PROSTATE**

AU Eymard J.-C.; Bernard J.

CS J.-C. Eymard, U. Fonct. Rech. Clin./Therapie Cell., Institut
 Jean-Godinot, 1, av. du gen. Koenig, 51056 Reims Cedex, France.
 E-mail: jc.eynard@reims.fnclcc.fr

SO Bulletin du Cancer, (2003), 90/8-9 (734-743), 63 reference(s)
 CODEN: BUCABS ISSN: 0007-4551

DT Journal; General Review

CY France

LA French

SL English; French

AB Hormonotherapy is the standard treatment for advanced **prostate cancer** but disease progression ineluctably occurs. Subsequent chemotherapy has a modest symptomatic palliative role even if encouraging results were recently presented with docetaxel and estramustine combination. In this context, there is a great deal of interest in using dendritic cells therapeutically, as they are the most potent professional antigen-presenting cells in the immune system. Based on their unique adjuvant capacity, two vaccinal strategies are therefore tested in clinical trials. First approach includes the administration of **cancer** cells transduced by a cytokine gene to stimulate the in vivo recruitment and activation of dendritic cells, and the most advanced studies use **GM-CSF** gene-transduced allogenic cells. The second approach consists in infusions of dendritic cells loaded ex vivo with relevant tumoral antigens. Two **prostate** antigens have already been used, PSMA evaluated in 130 patients and a fusion protein **PAP-GM-CSF** (Provenge®) in 144 patients. All treatments were well tolerated and frequently generated weak specific responses, but resulted in a limited clinical efficacy. However, engineering of dendritic cells can provide optimised cell vectors able to

amplify vaccine response and clinical efficacy.

L4 ANSWER 11 OF 17 Elsevier BIOBASE COPYRIGHT 2006 Elsevier Science B.V.
on STN
AN 2005226190 ESBIOBASE
TI Session II: Tumor antigens - **Prostate cancer** antigens
and vaccines
AU Salgaller M.L.; Elgamal A.-A.; Bosch M.; Lodge A.; Shankar G.; Boynton
A.; Belldegrun A.; Logothetis C.; Papandreou C.
CS Dr. M.L. Salgaller, Northwest Biotherapeutics, Inc., Seattle, WA, United
States.
SO Cancer Immunology, Immunotherapy, (2003), 52/SUPPL. 1 (S8-S9+S27)
CODEN: CIIMDN ISSN: 0340-7004
DT Journal; Conference Article
CY Germany, Federal Republic of
LA English
SL English
AB The clinical development of **prostate cancer** vaccines
presents several challenges. Reagents are more limited and difficult to
obtain as compared with other tumor types. The advanced age of the
patient population presents the researcher with subjects having
diminished immune systems and who are often less willing to undergo
procedures for research purposes. Consequently, the majority of research
has involved those **cancers** for which tumor and immune cells are
readily available. Despite these hurdles, new and novel approaches are
improving the poor overall survival rates through the development of
antigen-based treatment options. These efforts are particularly important
in the realm of hormone-refractory **prostate cancer**
(HRPC), since no therapy exists with significant clinical impact. This is
a major issue for the 36,000 men who will die from the disease annually,
despite transient responses to secondary treatment such as hormone
ablation therapy. During the past few years, candidate target antigens
for experimental vaccines have been identified in several laboratories.
These include oncogenes, overexpressed proteins, and carbohydrates. Three
of the furthest in clinical development are well-established clinical
markers of **prostate cancer**: **prostate**
-specific membrane antigen (PSMA), **prostate**-specific antigen
(PSA), and prostatic acid phosphatase (PAP). Following
conclusive preclinical evidence indicating that the human body responds
immunologically to **prostate** antigens, clinical trials have been
underway for many years with PSMA, PSA, and PAP as targets. We
investigated the capacity of a vaccine composed of autologous dendritic
cells (DC), pulsed ex vivo with recombinant PSMA (rPS-MA), to safely
generate clinically meaningful antitumor immune responses in HRPC
patients. In 2000 and 2001, 32 patients with metastatic or non-metastatic
HRPC were enrolled in a phase I/II clinical trial. Their peripheral blood
mononuclear cells were isolated by leukapheresis, matured to DC by in
vitro culture with maturation factors (GM-CSF, IL-4,
and inactivated BCG) for up to 7 days, followed by rPSMA loading and
harvesting of the vaccine. Patients received four intradermal treatments
of 5, 10, or 20-million rPSMA-loaded mature DC at monthly intervals,
followed by up to a total of 6 months of observation. Measurement of
serum anti-PSMA antibodies, PSMA-stimulated lymphocyte proliferation, and
delayed-type hypersensitivity (DTH) skin testing were carried out before,
during, and after vaccination. Clinical responses were assessed by
CT/bone scans and hematochemical laboratory tests, including PSA levels.
More than 140 total vaccine injections were well tolerated; no clinical
signs of autoimmunity or serious adverse events were observed. Overall,
54% of patients achieved stability of their disease at >6 months
follow-up, as assessed by radiographic criteria, and 83% of patients had
a PSMA-specific immune response, 92% of patients with stable disease had
a PSMA-specific immune response, and 46% of patients had a decrease in
PSA velocity. Compared to baseline, 93% of 27 evaluable patients
converted to DTH-positive against the BCG component of the vaccine. Due

to these promising initial findings we have initiated a double-blind, placebo-controlled phase III clinical trial. .COPYRG. 2002 Northwest Biotherapeutics, Inc. All rights reserved.

L4 ANSWER 12 OF 17 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2002-15068 BIOTECHDS
TI Eliciting or enhancing immune response to human self tumor antigen e.g.
HER-2/neu protein for preventing tumor occurrence by immunizing
individual with foreign protein or its portion homologous to the self
antigen;
recombinant vaccine against cancer
AU CHEEVER M A; DISIS M L
PA CHEEVER M A; DISIS M L
PI US 2002019331 14 Feb 2002
AI US 1996-88951 1 Apr 1996
PRAI US 1998-88951 2 Jun 1998
DT Patent
LA English
OS WPI: 2002-303155 [34]
AN 2002-15068 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - Eliciting or enhancing an immune response to a human self tumor
antigen involves immunizing a human being with a foreign protein
homologous to the antigen or with a foreign peptide homologous to a
portion of the antigen.
BIOTECHNOLOGY - Preferred Method: The foreign protein or peptide is
present in a carrier or diluent. The method additionally involves the use
of an adjuvant.
ACTIVITY - Antitumor.
MECHANISM OF ACTION - Immune response enhancer or elicitor
(claimed). Rats (Fischer strain 344 (CDF (F-344)/CrIBR)) were immunized
with recombinant human HER-2/neu intracellular domain protein (hICD) (50
microg) or immunoaffinity column purified rat neu protein (50 microg).
Proteins were administered with either complete Freund's antigen (CFA) or
murine granulocyte macrophage-colony stimulating factor (GM-
CSF) 5 microg as adjuvants. Control groups received adjuvant
alone. Animals underwent immunizations each 14-16 days apart. 18-10 days
after the second immunizations animals were assessed for immunologic
response. Rats immunized with hICD developed high titer human and rat neu
specific antibodies. All rats immunized with hICD developed significant
antibody responses specific for human HER-2/neu protein, with titers
greater than 1:200,000. Human HER-2/neu ICD is 92% homologous to rat neu
ICD at the amino acid level. Analysis was performed to discern whether
the human HER-2/neu specific antibodies were cross-reactive with rat neu.
Rats immunized with hICD with either GM-CSF or CFA as
an adjuvant had high titer antibody responses specific for rat neu. The
magnitude of the rat neu specific antibody responses was nearly identical
to that of the human HER-2/neu specific response. Delayed type
hypersensitivity (DTH) responses were used to initially evaluate for the
presence of the T cell responses to neu in rats immunized with HER-2/neu.
HER-2/neu specific DTH responses were detected in animals who received
hICD in GM-CSF or CFA. The responses were
cross-reactive to rat neu protein. DTH was not detected in animals
immunized with rat neu protein or with adjuvants alone. Immunization of
rats with hICD elicits detectable T cell responses specific for both
human and rat neu protein. T cell proliferative responses were evaluated
in rats immunized with hICD plus either GM-CSF or
CFA. T cell responses to hICD protein were detected from lymph nodes
draining the inoculation site. T cell responses to rat neu protein were
also detected, although at a lower magnitude than the hICD response.
USE - For eliciting or enhancing an immune response to a human self
tumor antigen which a protein expression product of an over expressed
human oncogene such as HER-2/neu protein, or a portion of the human
HER-2/neu protein, where the portion includes the intracellular domain of

the human HER-2/neu protein. Optionally the immune response is elicited or enhanced against an antigen or antigen portion which is an organ-specific or tissue-specific differentiation antigen associated with tumor cells, or a portion of the antigen. Preferably the organ- or tissue-specific differentiation antigen is an antigen associated with **prostate cancer**, e.g. prostatic acid phosphatase (PAP) or **prostate specific antigen (PSA)** (all claimed). The method is useful for eliciting or enhancing an immune response as a preventing measure to prevent tumor occurrence or recurrence, or as therapy to arrest tumor growth or eradicate existence tumors or to prolong the survival.

ADMINISTRATION - The vaccine composition is administered by intradermal, subcutaneous or intravenous routes. Dosages range from 1 microg/kg-1 mg/kg, preferably 5-200 microg/kg.

ADVANTAGE - The method overcomes immunological tolerance which exists and represents a potential barrier to effectively vaccinating against human self tumor antigens, by immunizing an individual with a protein or peptide that is foreign (i.e., not identical to that in the individual) but nevertheless homologous to an individuals self tumor antigen or its portion. (26 pages)

L4 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2001:417000 CAPLUS

DN 135:32745

TI Antigen-binding fragments specific for tumor associated antigens

IN Dan, Michael; Entwistle, Joycelyn; Fast, Darren; Kaplan, Howard; Lewis, Keith; MacDonald, Glen; Maiti, Pradip

PA Novopharm Biotech Inc., Can.

SO PCT Int. Appl., 176 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001040292	A1	20010607	WO 1999-CA1141	19991129
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRAI WO 1999-CA1141 19991129

AB The present invention relates to antigen-binding fragments that are specific for stress protein-peptide complexes specifically associated with tumors, particularly human tumors, and compns. thereof. The compns. are suitable for diagnostic and pharmaceutical use. The invention further provides methods of making and screening for the antigen-binding fragments. The invention further encompasses compns. containing **cancer**-associated stress protein-peptide complexes (including derivs. thereof) and methods of use thereof. The **cancer**-specific stress protein-peptide complexes (SPPC's) are particularly useful in eliciting **cancer**-specific immunogenic responses against a plurality of **cancers**. The invention also provides novel phage display libraries for use in producing further SPPCs and anti-SPPCs of the invention.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2001:224352 CAPLUS

DN 134:251211
 TI Monoclonal antibody to C-antigen: Prophylaxis and detection of
cancer
 IN Dan, Michael D.; Maiti, Pradip K.; Kaplan, Howard A.
 PA Viventia Biotech, Inc., Can.
 SO U.S., 56 pp., Cont.-in-part of U.S. Ser. No. 657,449, abandoned.
 CODEN: USXXAM
 DT Patent
 LA English
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6207153	B1	20010327	US 1997-862124	19970522
	CA 2255540	AA	19971127	CA 1997-2255540	19970522
	CN 1229436	A	19990922	CN 1997-194815	19970522
	NZ 505305	A	20020628	NZ 1997-505305	19970522
	KR 2000015893	A	20000315	KR 1998-709444	19981121
	AU 775448	B2	20040729	AU 2000-72432	20001220
	US 2003021779	A1	20030130	US 2001-782397	20010213
	US 2004091484	A1	20040513	US 2003-651453	20030829
PRAI	US 1996-657449	B2	19960522		
	AU 1997-33696	A3	19970522		
	NZ 1997-332566	A1	19970522		
	US 1997-862124	A1	19970522		
	US 2001-782397	B1	20010213		

AB The authors disclose preparation and sequence characterization of monoclonal antibody H11 that specifically binds to an antigen (termed "C-antigen") expressed by diverse tumors and tumor cell lines. The C-antigen was not found on normal cells. Also disclosed are polynucleotides and single chain antibodies based on H11 for application in therapy and tumor imaging.

RE.CNT 124 THERE ARE 124 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2004:869162 CAPLUS
 DN 142:233296
 TI Consensus peptide presenting entities, screening methods, and use for the treatment and diagnosis of tumors.
 IN Maiti, Pradip K.; Herman, William; Dan, Michael D.; Kaplan, Howard A.; MacDonald, Glen C.; Entwistle, Jocelyn M.; Lewis, Keith E.; Fast, Darren G.
 PA Novopharm Biotech Inc., Can.
 SO Can. Pat. Appl., 155 pp.
 CODEN: CPXXEB

DT Patent
 LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CA 2290722	AA	20010608	CA 1999-2290722	19991208
PRAI	CA 1999-2290722		19991208		

AB The invention provides antigen-binding-fragments specific for tumor cells and effective in treatment and/or diagnosing tumors. Methods of use are also provided as are methods for screening for addnl. such antigen-binding-fragments and the products obtained thereby.

L4 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2000:445203 CAPLUS
 DN 133:87934
 TI Priming tissue-specific cellular immunity in a phase I trial of autologous dendritic cells for **prostate cancer**
 AU Burch, Patrick A.; Breen, Jami K.; Buckner, Jan C.; Gastineau, Dennis A.; Kaur, Judith A.; Laus, Reiner L.; Padley, Douglas J.; Peshwa, Madhusudan

V.; Pitot, Henry C.; Richardson, Ronald L.; Smits, Bouwien J.; Sopapan, Pitsata; Strang, George; Valone, Frank H.; Vuk-Pavlovic, Stanimir
CS Divisions of Medical Oncology, Mayo Clinic and Mayo Foundation, Rochester, MN, 55905, USA
SO Clinical Cancer Research (2000), 6(6), 2175-2182
CODEN: CCREF4; ISSN: 1078-0432

PB American Association for Cancer Research

DT Journal

LA English

AB We attempted to induce therapeutic immunity against **prostate**-derived tissues in patients suffering from progressive hormone-refractory metastatic **prostate** carcinoma. Thirteen patients were treated with two infusions, 1 mo apart, of autologous dendritic cells (APC8015) preexposed ex vivo to PA2024, a fusion protein consisting of human granulocyte/macrophage-colony stimulating factor (**GM-CSF**) and human prostatic acid phosphatase (**PAP**). The infusions were followed by three s.c. monthly doses of PA2024 without cells. Three groups of patients each received PA2024 at 0.3, 0.6, or 1.0 mg/injection. All Ps were two-sided. Treatment was well tolerated. After infusions of APC8015, patients experienced only mild (grade 1-2) short-lived fever and/or chills, myalgia, pain, and fatigue. One patient developed grade 3 fatigue. Four patients developed mild local reactions to s.c. PA2024. Twelve patients were evaluable for response to treatment. Circulating **prostate**-specific antigen levels dropped in three patients. T cells, drawn from patients after infusions of APC8015, but not before, could be stimulated in vitro by **GM-CSF** ($P = 0.0004$) and **PAP** ($P = 0.0001$), demonstrating broken immune tolerance against these two normal proteins. Injections of PA2024 did not influence the reactivity of T cells against **PAP** and **GM-CSF**. However, antibodies to **GM-CSF** and, to a much lesser extent, to **PAP** reached maximum titers only after two or even three injections of PA2024, showing that directly injected PA2024 was involved in stimulation of humoral immunity. Dendritic cells exposed to antigen ex vivo can induce antigen-specific cellular immunity in **prostate cancer** patients, warranting further studies of this mode of immunotherapy.

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2000:444894 CAPLUS

DN 134:84982

TI PSA is a candidate self-antigen in autoimmune chronic prostatitis/chronic pelvic pain syndrome

AU Ponniah, Sathibalan; Arah, Ifeyinwa; Alexander, Richard B.

CS Division of Urology, University of Maryland School of Medicine, Baltimore, MD, USA

SO Prostate (New York) (2000), 44(1), 49-54

CODEN: PRSTDS; ISSN: 0270-4137

PB Wiley-Liss, Inc.

DT Journal

LA English

AB BACKGROUND. Previous studies demonstrated that recognition of seminal plasma antigens can occur in patients with chronic prostatitis/chronic pelvic pain syndrome. This suggests that an autoimmune component may contribute to symptoms in some men. To determine if any of the principal secretory proteins of the **prostate** could be candidate antigens in auto-immune prostatitis, we examined the recall proliferative response of purified CD4 T cells in patients with chronic prostatitis and in normal volunteers using purified seminal plasma antigens and autologous dendritic cells. METHODS. Peripheral blood mononuclear cells were harvested from 14 patients with chronic prostatitis and 12 normal volunteers by d. gradient centrifugation. The stimulating cells were irradiated autologous dendritic cells produced by culture of monocyte-enriched fractions with

IL-4 and Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF). Purified CD4 T cells were the responding population. Recall proliferation assays were performed, using purified seminal plasma proteins as antigens. RESULTS. In 14 patients with chronic prostatitis, we detected a greater than 2-fold increase in proliferative response to PSA compared to control in 5 patients (36%). No response to Prostatic Acid Phosphatase (PAP) or β -microseminoprotein was observed in these 14 patients. In 12 normal volunteer donors with no history of genitourinary disease or symptoms, no proliferative response above background was observed for any prostatic antigen. CONCLUSIONS. The data suggest that some men with symptoms of chronic prostatitis have evidence of a proliferative CD4 T-cell response to PSA. PSA is a candidate antigen in chronic prostatitis/chronic pelvic pain syndrome and may be an appropriate target for immunotherapy for prostatic cancer.

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 11:57:08 ON 21 JUN 2006)

FILE 'CAPLUS, BIOENG, BIOTECHNO, BIOTECHDS, ESBIODBASE' ENTERED AT
11:57:29 ON 21 JUN 2006

L1 31 S (PAP AND (GM (W) CSF) AND CANCER)
L2 25 DUPLICATE REMOVE L1 (6 DUPLICATES REMOVED)
L3 17 S (L2 AND PROSTATE)
L4 17 DUPLICATE REMOVE L3 (0 DUPLICATES REMOVED)

=> d 12 bib abs 1-25

L2 ANSWER 1 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
AN 2005:1321617 CAPLUS
TI Safety and immunological efficacy of a prostate cancer plasmid
DNA vaccine encoding prostatic acid phosphatase (PAP)
AU Johnson, Laura E.; Frye, Thomas P.; Arnot, Alana R.; Marquette, Carrie;
Couture, Larry A.; Gendron-Fitzpatrick, Annette; McNeel, Douglas G.
CS Department of Medicine, Section of Medical Oncology, K4/518 Clinical
Science Center, University of Wisconsin-Madison, Madison, WI, 53792, USA
SO Vaccine (2006), 24(3), 293-303
CODEN: VACCDE; ISSN: 0264-410X
PB Elsevier B.V.
DT Journal
LA English
AB Prostatic acid phosphatase (PAP) is a prostate tumor antigen currently being investigated as a target antigen in several human vaccine trials, some with evidence of clin. benefit. We have previously demonstrated that plasmid DNA vaccines encoding either human or rat PAP can elicit antigen-specific cellular and humoral immunity in rat models. The current study was performed to determine the safety and potential immunol. efficacy in rodents of large and repetitive doses of a GMP-grade plasmid DNA vaccine encoding human PAP, pTVG-HP. Fifty-four male Lewis rats were immunized intradermally at 2-wk intervals with 100, 500, or 1500 μ g pTVG-HP with 5 μ g recombinant rat GM-CSF protein given as a vaccine adjuvant. An addnl. 12 male Lewis rats served as controls with groups immunized with 1500 μ g of a parental DNA vector not encoding human PAP, and a group that received GM-CSF protein only without plasmid DNA. Groups of animals (n = 3-6) were euthanized after two, four, or six immunizations with collections of tissues and blood for toxicity assessment and immunol. anal. No significant toxicities were observed in terms of animal wts., histopathol., hematol. changes, or changes in serum chemistries. Six of fifty-four were found to have subtle evidence of possible renal toxicity, however these findings were not statistically

different from control animals. The vaccine was found to be effective in eliciting PAP-specific CD4 and CD8 T cells, predominantly Th1 in type, in all immunized animals at all doses and nos. of immunizations. PAP-specific IgG were detected in a dose-dependent fashion, with titers increasing after multiple immunizations. These studies demonstrate that, in rats, immunization with the pTVG-HP vaccine is safe and effective in eliciting PAP-specific cellular and humoral immune responses. These findings support the further clin. evaluation of pTVG-HP in patients with prostate cancer.

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:72938 CAPLUS
TI Provenge: prostate cancer therapy
AU McIntyre, J. A.; Fernandez, D.
CS Prous Science, Barcelona, 08080, Spain
SO Drugs of the Future (2005), 30(9), 892-895
CODEN: DRFUD4; ISSN: 0377-8282
PB Prous Science
DT Journal; General Review
LA English
AB A review. There are few therapeutic options available for the treatment of hormone-refractory prostate cancer (HRPC), but recent advancements in the understanding of immune recognition have resulted in the development of novel vaccine products aimed at inducing prostate-specific T-cell-mediated immunity. Provenge (APC-8015) is an immunotherapeutic consisting of autologous dendritic cell precursors loaded ex vivo with a recombinant fusion protein (PA2024) comprising prostatic acid phosphatase (PAP), an antigen found in 95% of prostate cancers, and granulocyte-macrophage colony-stimulating factor (GM-CSF). Early clin. studies demonstrated good tolerability of the product and T-cell proliferation responses to PA2024. Phase II studies indicated the preliminary efficacy of Provenge, with increases in prostate-specific antigen (PSA) doubling time and PSA-modulating effects. Subsequent placebo-controlled phase III studies identified advantages for Provenge in terms of time to disease progression and time to onset of disease-related pain.

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:1127402 CAPLUS
DN 142:54751
TI Alternative reading frame peptides as antigens for the prophylaxis and treatment of cancer and infectious diseases
IN Graddis, Thomas; Laus, Reiner; Diegel, Michael; Vidovic, Damis
PA Dendreon Corporation, USA
SO PCT Int. Appl., 147 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004111075	A2	20041223	WO 2004-US6979	20040305
	WO 2004111075	C1	20050519		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,			

BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
TD, TG

CA 2514288 AA 20041223 CA 2004-2514288 20040305
US 2005112134 A1 20050526 US 2004-794514 20040305
EP 1601684 A2 20051207 EP 2004-749357 20040305

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK

PRAI US 2003-453131P P 20030305
WO 2004-US6979 W 20040305

AB Alternative reading frame (ARF) peptides associated with disease conditions and that can be recognized by antigen presenting cells (APC) and dendritic cells (DC) are described for use as antigens in the diagnosis, treatment, and prevention of diseases including **cancer** and infectious diseases. These peptides may arise from frameshifting, use of alternative start codons, ribosomal skipping, suppression of termination of translation, translation of antisense transcripts, splice variants or use of cryptic promoters. Alternative reading frame peptides derived from the HER-2 receptor gene were incubated with mouse dendritic cells in vitro and the cells reintroduced into the donor mice. Mice challenged with B16 cells blocked tumor growth, whereas animals treated with inframe HER-2 proteins did not.

L2 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:333598 CAPLUS

DN 140:373894

TI CEA-specific monoclonal antibodies or fragments with therapeutic agents for treating CEA-expressing **cancers** and diseases

IN Goldenberg, David M.; Hansen, Hans J.

PA Immunomedics, Inc., USA

SO PCT Int. Appl., 88 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004032962	A1	20040422	WO 2002-US32307	20021011
	W:			AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW	
	RW:			GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG	
	CA 2501757	AA	20040422	CA 2002-2501757	20021011
	AU 2002332087	A1	20040504	AU 2002-332087	20021011
	EP 1558284	A1	20050803	EP 2002-769028	20021011
	R:			AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK	
	JP 2006507263	T2	20060302	JP 2004-542990	20021011
	CA 2501616	AA	20040422	CA 2003-2501616	20031008
	WO 2004032857	A2	20040422	WO 2003-US31801	20031008
	WO 2004032857	C1	20050407		
	W:			AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW	

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003282752 A1 20040504 AU 2003-282752 20031008
 US 2004191248 A1 20040930 US 2003-680734 20031008
 EP 1572131 A2 20050914 EP 2003-774636 20031008

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRAI US 2002-416531P P 20021008
 WO 2002-US32307 W 20021011
 US 2003-467161P P 20030502
 WO 2003-US31801 W 20031008

AB The present invention provides a composition comprising naked humanized, chimeric and human Class III anti-CEA monoclonal antibody and a therapeutic agent, which is useful for treatment of CEA-expressing **cancers** and other diseases, and methods of treatment using this composition. The anti-CEA monoclonal antibody or fragment is a humanized or chimeric MN-14 antibody or fragment or fully human MN-14 antibody or fragment.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2004:331925 CAPLUS
 DN 140:355848
 TI humanized or chimeric derivatives of murine monoclonal anti-CEA antibody MN-14 and conjugates for **cancer** therapy
 IN Goldenberg, David M.; Hansen, Hans J.
 PA Immunomedics, Inc., USA
 SO PCT Int. Appl., 121 pp.
 CODEN: PIXXD2

DT Patent
 LA English

FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004032857	A2	20040422	WO 2003-US31801	20031008
WO 2004032857	C1	20050407		
W:				
AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW:				
GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2004032962	A1	20040422	WO 2002-US32307	20021011
W:				
AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW:				
GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2501616	AA	20040422	CA 2003-2501616	20031008
AU 2003282752	A1	20040504	AU 2003-282752	20031008
EP 1572131	A2	20050914	EP 2003-774636	20031008
R:				
AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRAI US 2002-416531P P 20021008
 WO 2002-US32307 A 20021011
 US 2003-467161P P 20030502
 WO 2003-US31801 W 20031008

AB The present invention provides a composition comprising naked humanized or chimeric murine monoclonal antibody MN-14 and a therapeutic agent, which is useful for treatment of CEA expressing **cancers** and other diseases, and methods of use in treatment using this composition

L2 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2004:287861 CAPLUS
 DN 140:320038
 TI Chimeric and humanized anti-granulocyte antibodies, immunoconjugates and labeled antibodies for diagnosis and treatment of malignancy, infection and inflammation
 IN Goldenberg, David M.; Hansen, Hans; Leung, Shui-on
 PA Immunomedics, Inc., USA; Mccall, John Douglas
 SO PCT Int. Appl., 134 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004029093	A2	20040408	WO 2003-GB4229	20030930
	WO 2004029093	A3	20040603		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	CN 1542019	A	20041103	CN 2003-123054	20030429
	CA 2500250	AA	20040408	CA 2003-2500250	20030930
	AU 2003269225	A1	20040419	AU 2003-269225	20030930
	EP 1546204	A2	20050629	EP 2003-751001	20030930
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
PRAI	US 2002-414341P	P	20020930		
	WO 2003-GB4229	W	20030930		

DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004026238	A2	20040401	WO 2003-US29176	20030919
	WO 2004026238	C1	20040722		
	WO 2004026238	A3	20041209		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	CA 2497554	AA	20040401	CA 2003-2497554	20030919
	AU 2003267254	A1	20040408	AU 2003-267254	20030919
	US 2004161413	A1	20040819	US 2003-666122	20030919
	EP 1540627	A2	20050615	EP 2003-749725	20030919
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
PRAI	US 2002-412271P	P	20020920		
	US 2003-475355P	P	20030602		
	US 2003-475335P	P	20030602		
	WO 2003-US29176	W	20030919		
AB	<p>The invention discloses immunotherapeutic compns. comprising activated antigen presenting cells (APCs), wherein said APCs were obtained from cancer patients and stimulated by exposure ex vivo to a fusion protein composed of a APC binding protein and tumor-associated (specific) antigen. The invention also discloses the use of said stimulated/activated APCs in treatment of patients with moderately to well-differentiated cancer cells. The invention further provides a method of assessing in cancer patients the susceptibility of cancer to said immunotherapeutic compns. As way of illustration, the invention discloses a fusion protein (APC8015) composed of a portion of prostate tumor-associated protein human prostatic acid phosphatase (huPAP) at the N-terminus and a portion of APC/DC binding protein human granulocyte-macrophage colony stimulating factor (huGM-CSF) at the C-terminus. APC stimulated by exposure ex vivo to said PAP /GM-CSF fusion protein were effective in activating T cells to produce a cytotoxic cellular response against huPAP. Finally, the invention discloses the amino acid sequences of huPAP and huGM-CSF. In the examples, the invention demonstrated that the therapeutic efficacy of immunotherapeutic compns. comprising APCs stimulated with PAP /GM-CSF fusion protein correlates with the differentiation state of the prostate cancer cells. Specifically, it was demonstrated that patients exhibiting moderately to well-differentiated prostate cancer cells were susceptible to treatment with said immunotherapeutic composition. The invention also demonstrated the efficacy of a combined immunotherapeutic treatment regimen that includes administration of PAP/GM-CSF-pulsed dendritic cells in conjunction with administration of humanized anti-VEGF monoclonal antibody Bevacizumab in patients having a serol. progression of prostate cancer.</p>				
L2	ANSWER 8 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN				
AN	2004:120888 CAPLUS				
DN	140:198085				
TI	Chimeric and humanized anti- α -fetoprotein antibodies Immu31 and fragments for diagnosis and therapy of hepatocellular carcinoma, hepatoblastoma and germ cell tumors				

IN Hansen, Hans; Qu, Zhengxing; Goldenberg, David M.
PA Immunomedics, Inc., USA; McCall, John Douglas
SO PCT Int. Appl., 155 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004013180	A2	20040212	WO 2003-GB3325	20030801
	WO 2004013180	A3	20040916		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	CA 2494310	AA	20040212	CA 2003-2494310	20030801
	AU 2003248982	A1	20040223	AU 2003-248982	20030801
	US 2004235065	A1	20041125	US 2003-631722	20030801
	EP 1546203	A2	20050629	EP 2003-766456	20030801
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
PRAI	US 2002-399707P	P	20020801		
	WO 2003-GB3325	W	20030801		

AB The present invention provides humanized, chimeric and human anti-alpha-fetoprotein antibodies, fusion proteins, and fragments thereof. The antibodies, fusion proteins, and fragments thereof, as well as combinations with other suitable antibodies, are useful for the treatment and diagnosis of hepatocellular carcinoma, hepatoblastoma, germ cell tumors, carcinoma and other AFP-producing tumors.

L2 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:589231 CAPLUS
DN 141:134058
TI Methods and compositions for treating prostate cancer using DNA vaccines
IN McNeel, Douglas
PA Wisconsin Alumni Research Foundation, USA
SO U.S. Pat. Appl. Publ., 39 pp.
CODEN: USXXCO

DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004142890	A1	20040722	US 2003-669474	20030925
PRAI	US 2002-413777P	P	20020927		
AB	A DNA vaccine for the treatment of prostate cancer, comprising a plasmid vector comprising a nucleotide sequence encoding prostatic acid phosphatase (PAP) operably linked to a transcription regulatory element, wherein upon administration to a mammal a cytotoxic immune reaction against cells expressing PAP is induced. In preferred embodiment, the PAP encoded is a xenoantigen highly homologous to the autoantigen PAP of the mammal. Also disclosed are methods for inducing prostatitis, or inducing immune reaction to PAP, or treating prostate cancer in a mammal, using the DNA vaccine and pharmaceutical compns. comprising the vaccine. Preferably, xenoantigen vaccination is followed by boosting with autoantigen PAP from the same animal species as the mammal being				

treated. Lewis rats immunized with pTVG-HP, encoding human PAP, developed PAP-specific cellular immunity and prostate tissue inflammation.

L2 ANSWER 10 OF 25 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2004-21964 BIOTECHDS
TI Treating **cancer** with an immunotherapeutic composition comprises determining differentiation state of **cancer** cells, where presence of moderately to well-differentiated cells indicates patient susceptible to treatment with the composition;
composition for **cancer** immunotherapy comprises dendrite cell exposed to tumor-associated antigen
AU LAUS R; GOLD M H; PESHA M; PICKERING G; KYLSTRA J
PA DENDREON CORP
PI US 2004161413 19 Aug 2004
AI US 2003-666122 19 Sep 2003
PRAI US 2003-666122 19 Sep 2003; US 2002-412271 20 Sep 2002
DT Patent
LA English
OS WPI: 2004-614827 [59]
AN 2004-21964 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - Treating (M1) a **cancer** patient with an immunotherapeutic composition where the patient has a **cancer** with moderately to well-differentiated **cancer** cells, comprising determining the differentiation state of the **cancer** cells, where the presence of moderately to well-differentiated **cancer** cells indicates a patient susceptible to treatment with an immunotherapeutic composition, and administering the composition, where a reduction of 10% indicates an effective treatment of the **cancer**, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an immunotherapeutic composition (I) comprising activated, isolated antigen presenting cells (APCs) that are obtained from a patient diagnosed with a **cancer** having a moderate to well-differentiated **cancer** grade and are stimulated by exposure ex vivo to a tumor-associated antigen (TAA); (2) inhibiting (M2) growth of a **cancer** cell in a patient having a moderate to well-differentiated **cancer** grade, comprising determining the differentiation state of the **cancer** cells, where the presence of moderately to well-differentiated **cancer** cells indicates a patient susceptible to treatment, isolating APCs from the patient, stimulating the APCs by exposure ex vivo to the immunotherapeutic composition comprising a protein conjugate having an N-terminal moiety and a C-terminal moiety, where the APCs are effective to activate T-cells to produce a cytotoxic cellular response against either the N-terminal moiety or the C-terminal moiety and where the level of the T-cell activation is higher than that produced by the APCs when exposed exclusively to the N- or C-terminal moiety, and administering to the patient the stimulated APCs, where a reduction of 10% indicates an effective treatment of the **cancer** and (3) a method of assessing in a **cancer** patient the susceptibility of the **cancer** to an immunotherapeutic composition, comprising isolating from the patient a sample containing the **cancer** cell, and determining the differentiation state of the **cancer** cell, where a moderate to well-differentiated **cancer** grade indicates that the **cancer** is susceptible to treatment with an immunotherapeutic composition.
WIDER DISCLOSURE - Also disclosed are nucleic acids, polypeptides, host cells, vectors and antibodies used in the methods of the invention.
BIOTECHNOLOGY - Preferred Method: The composition is (I). Preferred Composition: The TAA of the immunotherapeutic composition is a tumor-specific antigen, or is a component of a protein conjugate comprising an N- and C-terminal moiety. The APCs are dendritic cells. The

cancer is soft tissue sarcomas, lymphomas, and **cancers** of the brain, esophagus, uterine, cervix, bone, lung, endometrium, bladder, breast, larynx, colon/rectum, stomach, ovary, pancreas, adrenal gland or prostate. The **cancer** grade corresponds to a Gleason score of at most 7. The patient is not refractory to hormone ablation therapy. The N- or C-terminal moiety is an APC binding protein an/or a TAA. The fusion protein further comprises, between the N- and the C-terminal moiety, a linker peptide. The N- or C-terminal comprises a sequence having at least 70, 80, 90 or 100% identical to huPAP or huGM-CSF with a fully defined sequence of 386 or 144 amino acids (SEQ ID NO: 1 and 3), respectively, as given in the specification.

ACTIVITY - Cytostatic; Immunostimulant. Prior to initiating an immunotherapeutic treatment regimen with **PAP/GM-CSF** fusion protein (APC8015) or placebo, patients were assessed for baseline disease characteristics. To determine the differentiation state of prostate **cancer** cells, prostate tissue samples were isolated from each patient and subjected to analysis by the Gleason scoring methodology as described in Gleason, Urologic Pathology: The Prostate, pp. 171-197 (Tappenhaum, ed., Lee and Fehiger, Philadelphia, Pa., 1977). Time to objective disease progression was defined as progression on bone scan or x-ray or clinical deterioration and the data were subjected to statistical analysis by the Kaplan-Meier methodology. PSA was not used to determine disease progression. The median time to disease progression for the patient population treated with APC8015 was 11.0 weeks whereas the median time to disease progression for the patient population treated with placebo was 9.1 weeks. The data demonstrated that patients having poorly differentiated prostate **cancer** cells were refractory to treatment with APC8015 as evidenced by the absence of a statistically significant difference (p-value=0.431) in time to objective disease progression for the patient population treated with APC8015 as compared to the patient population treated with the placebo. In contrast, the results obtained for patients exhibiting moderately to well-differentiated prostate **cancer** cells (having a Gleason score of less than or equal to 7) show that such patients were susceptible to treatment with an immunotherapeutic composition as evidenced by the high degree of statistical significance (p-value=0.002) in time to objective disease progression for the patient population treated with APC8015 as compared to the patient population treated with the placebo.

MECHANISM OF ACTION - None given.

USE - For treating **cancers** including soft tissue sarcomas, lymphomas, and **cancers** of the brain, esophagus, uterine, cervix, bone, lung, endometrium, bladder, breast, larynx, colon/rectum, stomach, ovary, pancreas, adrenal gland or prostate (claimed).

ADMINISTRATION - Routes of administration of the pharmaceutical compositions include oral, pulmonary, intramuscular, intraperitoneal, intravenous, subcutaneous, inhalation, transdermal, nasal, vaginal, rectal and sublingual. No dosages given.

ADVANTAGE - The method is based upon the observation that the grade of a **cancer** cell, being a measure of the cell's differentiation state, is predictive of clinical outcome in **cancer** patients undergoing an immunotherapeutic treatment regimen. Whereas poorly differentiated cells were found to be refractory to an immunotherapeutic treatment regimen, moderately to well-differentiated cells were highly susceptible to treatment with immunotherapeutic compositions. (34 pages)

L2 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:715711 CAPLUS

DN 141:294358

TI Immunotherapy (APC8015, Provenge) targeting prostatic acid phosphatase can induce durable remission of metastatic androgen-independent prostate **cancer**: a phase 2 trial

AU Burch, Patrick A.; Croghan, Gary A.; Gastineau, Dennis A.; Jones, Lori A.; Kaur, Judith S.; Kylastra, Jelle W.; Richardson, Ronald L.; Valone, Frank

H.; Vuk-Pavlovic, Stanimir
 CS Division of Medical Oncology, Department of Oncology, Mayo Clinic,
 Rochester, MN, USA
 SO Prostate (New York, NY, United States) (2004), 60(3), 197-204
 CODEN: PRSTDS; ISSN: 0270-4137
 PB Wiley-Liss, Inc.
 DT Journal
 LA English
 AB Prostate **cancer** is the most commonly diagnosed malignancy in American men, yet treatment of its metastatic androgen-independent form remains inadequate. This mandates development of new therapies such as immunotherapy. In this Phase 2 trial, we determined the efficacy of antigen presenting cells (APCs) loaded with PA2024, a recombinant fusion protein containing prostatic acid phosphatase (PAP) and GM-CSF. We enrolled 21 patients with histol. documented androgen-independent prostate carcinoma that could be evaluated by radionuclide bone scan or computed tomog. scan. APC8015 was prepared from a leukapheresis product; it contained autologous CD54-pos. PA2024-loaded APCs with admixts. of monocytes, macrophages, B and T cells. APC8015 was infused i.v. twice, 2 wk apart. Two weeks after the second infusion, patients received three s.c. injections of 1.0 mg of PA2024 1 mo apart. We monitored patients' phys. condition, immune response, and laboratory parameters. Nineteen patients could be evaluated for response to treatment. The median time to progression was 118 days. Treatment was tolerated reasonably well; most adverse effects were secondary to APC8015 and were NCI Common Toxicity Criteria Grade 1-2. Four of the 21 patients reported Grade 3-4 adverse events. Two patients exhibited a transient 25-50% decrease in prostate-specific antigen (PSA). For a third patient, PSA dropped from 221 ng/mL at baseline to undetectable levels by week 24 and has remained so for more than 4 yr. In addition, this patient's metastatic retroperitoneal and pelvic adenopathy has resolved. PBMC collected from patients for at least 16 wk proliferated upon in vitro stimulation by PA2024. For the patient with responsive disease, PBMC could be stimulated for 96 wk. This study demonstrates a definite clin. response of androgen-independent prostate **cancer** to APC immunotherapy. Currently we are studying this mode of therapy in Phase 3 trials.

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2
 AN 2003:719518 CAPLUS
 DN 139:259962
 TI Humanized murine anti-epithelial glycoprotein 1 (EGP-1) antibodies RS7 and conjugates for diagnosis and treatment of **cancer**
 IN Govindan, Serengulam; Qu, Zhengxing; Hansen, Hans J.; Goldenberg, David M.
 PA Immunomedics, Inc., USA; Mccall, John Douglas
 SO PCT Int. Appl., 97 pp.
 CODEN: PIXXD2

DT Patent
 LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003074566	A2	20030912	WO 2003-GB885	20030303
WO 2003074566	A3	20040304		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,				

FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG .

CA 2478047	AA	20030912	CA 2003-2478047	20030303
AU 2003209447	A1	20030916	AU 2003-209447	20030303
US 2004001825	A1	20040101	US 2003-377121	20030303
EP 1483295	A2	20041208	EP 2003-743420	20030303

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

CN 1649903	A	20050803	CN 2003-809918	20030303
JP 2006502698	T2	20060126	JP 2003-573031	20030303

PRAI US 2002-360229P P 20020301
WO 2003-GB885 W 20030303

AB This invention relates to monovalent and multivalent, monospecific binding proteins and to multivalent, multispecific binding proteins. One embodiment of these binding proteins has one or more binding sites where each binding site binds with a target antigen or an epitope on a target antigen. Another embodiment of these binding proteins has two or more binding sites where each binding site has affinity towards different epitopes on a target antigen or has affinity towards either a target antigen or a hapten. The present invention further relates to recombinant vectors useful for the expression of these functional binding proteins in a host. More specifically, the present invention relates to the tumor-associated antigen binding protein designated RS7, and other EGP-1 binding-proteins. The invention further relates to humanized, human and chimeric RS7 antigen binding proteins, and the use of such binding proteins in diagnosis and therapy.

L2 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:1007015 CAPLUS
DN 140:58438
TI Monoclonal anti-MUC1 antibody PAM4 and chimeric antibodies for diagnosis and therapy of pancreatic cancer
IN Gold, David V.; Goldenberg, David M.; Hansen, Hans
PA Immunomedics, Inc., USA; McCall, John Douglas
SO PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2003106497 A1 20031224 WO 2003-GB2585 20030616

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR,
TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2489469	AA	20031224	CA 2003-2489469	20030616
AU 2003250367	A1	20031231	AU 2003-250367	20030616
US 2004057902	A1	20040325	US 2003-461878	20030616
EP 1521775	A1	20050413	EP 2003-760086	20030616

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

JP 2006507803	T2	20060309	JP 2004-513328	20030616
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PRAI US 2002-388313P P 20020614
WO 2003-GB2585 W 20030616

AB This invention relates to monovalent and multivalent, monospecific antibodies and to monovalent and multivalent, multispecific antibodies. One embodiment of these antibodies has one or more identical binding sites

where each binding site binds with a target antigen or an epitope on a target antigen. Another embodiment of these antibodies has two or more binding sites where these binding sites have affinity towards different epitopes on a target antigen or different target antigens, or have affinity towards a target antigen and a hapten. The present invention further relates to recombinant vectors useful for the expression of these functional antibodies in a host. More specifically, the present invention relates to the tumor-associated antibody designated PAM4. The invention further relates to chimeric PAM4 antibodies, and the use of such antibodies in diagnosis and therapy.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 14 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:1007014 CAPLUS
DN 140:58437
TI Multivalent humanized monoclonal anti-MUC1 antibody PAM4 for diagnosis and treatment of **cancer**
IN Goldenberg, David M.; Hansen, Hans; Qu, Zhengxing
PA Immunomedics, Inc., USA; McCall, John Douglas
SO PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003106495	A2	20031224	WO 2003-GB2593	20030616
	WO 2003106495	A3	20040401		
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2489467	AA	20031224	CA 2003-2489467	20030616
	AU 2003277087	A1	20031231	AU 2003-277087	20030616
	US 2005014207	A1	20050120	US 2003-461885	20030616
	EP 1519958	A2	20050406	EP 2003-740743	20030616
	R:				
	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	BR 2003011799	A	20050510	BR 2003-11799	20030616
	CN 1675245	A	20050928	CN 2003-819294	20030616
	JP 2006513695	T2	20060427	JP 2004-513326	20030616
PRAI	US 2002-388314P	P	20020614		
	WO 2003-GB2593	W	20030616		

AB This invention relates to monovalent and multivalent, monospecific antibodies and to multivalent, multispecific antibodies. One embodiment of these antibodies has one or more identical binding sites where each binding site binds with a target antigen or an epitope on a target antigen. Another embodiment of these antibodies has two or more binding sites where these binding sites have affinity towards different epitopes on a target antigen or different target antigens, or have affinity towards a target antigen and a hapten. The present invention further relates to recombinant vectors useful for the expression of these functional antibodies in a host. More specifically, the present invention relates to the tumor-associated antibody designated PAM4. The invention further relates to humanized and human PAM4 antibodies, and the use of such antibodies in diagnosis and therapy.

L2 ANSWER 15 OF 25 BIOTECHNO COPYRIGHT 2006 Elsevier Science B.V. on STN
 AN 2003:37239077 BIOTECHNO
 TI Cell therapy and prostate **cancer**
 THERAPIE CELLULAIRE ET **CANCER** DE LA PROSTATE
 AU Eymard J.-C.; Bernard J.
 CS J.-C. Eymard, U. Fonct. Rech. Clin./Therapie Cell., Institut
 Jean-Godinot, 1, av. du gen. Koenig, 51056 Reims Cedex, France.
 E-mail: jc.eymard@reims.fnclcc.fr
 SO Bulletin du Cancer, (2003), 90/8-9 (734-743), 63 reference(s)
 CODEN: BUCABS ISSN: 0007-4551
 DT Journal; General Review
 CY France
 LA French
 SL English; French
 AB Hormonotherapy is the standard treatment for advanced prostate
cancer but disease progression ineluctably occurs. Subsequent
 chemotherapy has a modest symptomatic palliative role even if encouraging
 results were recently presented with docetaxel and estramustine
 combination. In this context, there is a great deal of interest in using
 dendritic cells therapeutically, as they are the most potent professional
 antigen-presenting cells in the immune system. Based on their unique
 adjuvant capacity, two vaccinal strategies are therefore tested in
 clinical trials. First approach includes the administration of
cancer cells transduced by a cytokine gene to stimulate the in
 vivo recruitment and activation of dendritic cells, and the most advanced
 studies use **GM-CSF** gene-transduced allogenic cells.
 The second approach consists in infusions of dendritic cells loaded ex
 vivo with relevant tumoral antigens. Two prostate antigens have already
 been used, PSMA evaluated in 130 patients and a fusion protein
PAP-GM-CSF (Provence®) in 144 patients.
 All treatments were well tolerated and frequently generated weak specific
 responses, but resulted in a limited clinical efficacy. However,
 engineering of dendritic cells can provide optimised cell vectors able to
 amplify vaccine response and clinical efficacy.

L2 ANSWER 16 OF 25 Elsevier BIOBASE COPYRIGHT 2006 Elsevier Science B.V.
 on STN
 AN 2005226190 ESBIOBASE
 TI Session II: Tumor antigens - Prostate **cancer** antigens and
 vaccines
 AU Salgaller M.L.; Elgamal A.-A.; Bosch M.; Lodge A.; Shankar G.; Boynton
 A.; Belldegrun A.; Logothetis C.; Papandreou C.
 CS Dr. M.L. Salgaller, Northwest Biotherapeutics, Inc., Seattle, WA, United
 States.
 SO Cancer Immunology, Immunotherapy, (2003), 52/SUPPL. 1 (S8-S9+S27)
 CODEN: CIIMDN ISSN: 0340-7004
 DT Journal; Conference Article
 CY Germany, Federal Republic of
 LA English
 SL English
 AB The clinical development of prostate **cancer** vaccines presents
 several challenges. Reagents are more limited and difficult to obtain as
 compared with other tumor types. The advanced age of the patient
 population presents the researcher with subjects having diminished immune
 systems and who are often less willing to undergo procedures for research
 purposes. Consequently, the majority of research has involved those
cancers for which tumor and immune cells are readily available.
 Despite these hurdles, new and novel approaches are improving the poor
 overall survival rates through the development of antigen-based treatment
 options. These efforts are particularly important in the realm of
 hormone-refractory prostate **cancer** (HRPC), since no therapy
 exists with significant clinical impact. This is a major issue for the
 36,000 men who will die from the disease annually, despite transient
 responses to secondary treatment such as hormone ablation therapy. During

the past few years, candidate target antigens for experimental vaccines have been identified in several laboratories. These include oncogenes, overexpressed proteins, and carbohydrates. Three of the furthest in clinical development are well-established clinical markers of prostate cancer: prostate-specific membrane antigen (PSMA), prostate-specific antigen (PSA), and prostatic acid phosphatase (PAP). Following conclusive preclinical evidence indicating that the human body responds immunologically to prostate antigens, clinical trials have been underway for many years with PSMA, PSA, and PAP as targets. We investigated the capacity of a vaccine composed of autologous dendritic cells (DC), pulsed ex vivo with recombinant PSMA (rPS-MA), to safely generate clinically meaningful antitumor immune responses in HRPC patients. In 2000 and 2001, 32 patients with metastatic or non-metastatic HRPC were enrolled in a phase I/II clinical trial. Their peripheral blood mononuclear cells were isolated by leukapheresis, matured to DC by in vitro culture with maturation factors (GM-CSF, IL-4, and inactivated BCG) for up to 7 days, followed by rPSMA loading and harvesting of the vaccine. Patients received four intradermal treatments of 5, 10, or 20-million rPSMA-loaded mature DC at monthly intervals, followed by up to a total of 6 months of observation. Measurement of serum anti-PSMA antibodies, PSMA-stimulated lymphocyte proliferation, and delayed-type hypersensitivity (DTH) skin testing were carried out before, during, and after vaccination. Clinical responses were assessed by CT/bone scans and hematochemical laboratory tests, including PSA levels. More than 140 total vaccine injections were well tolerated; no clinical signs of autoimmunity or serious adverse events were observed. Overall, 54% of patients achieved stability of their disease at >6 months follow-up, as assessed by radiographic criteria, and 83% of patients had a PSMA-specific immune response, 92% of patients with stable disease had a PSMA-specific immune response, and 46% of patients had a decrease in PSA velocity. Compared to baseline, 93% of 27 evaluable patients converted to DTH-positive against the BCG component of the vaccine. Due to these promising initial findings we have initiated a double-blind, placebo-controlled phase III clinical trial. .COPYRGT. 2002 Northwest Biotherapeutics, Inc. All rights reserved.

L2 ANSWER 17 OF 25 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2002-15068 BIOTECHDS
TI Eliciting or enhancing immune response to human self tumor antigen e.g. HER-2/neu protein for preventing tumor occurrence by immunizing individual with foreign protein or its portion homologous to the self antigen;
recombinant vaccine against cancer
AU CHEEVER M A; DISIS M L
PA CHEEVER M A; DISIS M L
PI US 2002019331 14 Feb 2002
AI US 1996-88951 1 Apr 1996
PRAI US 1998-88951 2 Jun 1998
DT Patent
LA English
OS WPI: 2002-303155 [34]
AN 2002-15068 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - Eliciting or enhancing an immune response to a human self tumor antigen involves immunizing a human being with a foreign protein homologous to the antigen or with a foreign peptide homologous to a portion of the antigen.
BIOTECHNOLOGY - Preferred Method: The foreign protein or peptide is present in a carrier or diluent. The method additionally involves the use of an adjuvant.
ACTIVITY - Antitumor.
MECHANISM OF ACTION - Immune response enhancer or elicitor (claimed). Rats (Fischer strain 344 (CDF (F-344)/CrIBR)) were immunized with recombinant human HER-2/neu intracellular domain protein (hICD) (50

microg) or immunoaffinity column purified rat neu protein (50 microg). Proteins were administered with either complete Freund's antigen (CFA) or murine granulocyte macrophage-colony stimulating factor (GM-CSF) 5 microg as adjuvants. Control groups received adjuvant alone. Animals underwent immunizations each 14-16 days apart. 18-10 days after the second immunizations animals were assessed for immunologic response. Rats immunized with hICD developed high titer human and rat neu specific antibodies. All rats immunized with hICD developed significant antibody responses specific for human HER-2/neu protein, with titers greater than 1:200,000. Human HER-2/neu ICD is 92% homologous to rat neu ICD at the amino acid level. Analysis was performed to discern whether the human HER-2/neu specific antibodies were cross-reactive with rat neu. Rats immunized with hICD with either GM-CSF or CFA as an adjuvant had high titer antibody responses specific for rat neu. The magnitude of the rat neu specific antibody responses was nearly identical to that of the human HER-2/neu specific response. Delayed type hypersensitivity (DTH) responses were used to initially evaluate for the presence of the T cell responses to neu in rats immunized with HER-2/neu. HER-2/neu specific DTH responses were detected in animals who received hICD in GM-CSF or CFA. The responses were cross-reactive to rat neu protein. DTH was not detected in animals immunized with rat neu protein or with adjuvants alone. Immunization of rats with hICD elicits detectable T cell responses specific for both human and rat neu protein. T cell proliferative responses were evaluated in rats immunized with hICD plus either GM-CSF or CFA. T cell responses to hICD protein were detected from lymph nodes draining the inoculation site. T cell responses to rat neu protein were also detected, although at a lower magnitude than the hICD response.

USE - For eliciting or enhancing an immune response to a human self tumor antigen which a protein expression product of an over expressed human oncogene such as HER-2/neu protein, or a portion of the human HER-2/neu protein, where the portion includes the intracellular domain of the human HER-2/neu protein. Optionally the immune response is elicited or enhanced against an antigen or antigen portion which is an organ-specific or tissue-specific differentiation antigen associated with tumor cells, or a portion of the antigen. Preferably the organ- or tissue-specific differentiation antigen is an antigen associated with prostate cancer, e.g. prostatic acid phosphatase (PAP) or prostate specific antigen (PSA) (all claimed). The method is useful for eliciting or enhancing an immune response as a preventing measure to prevent tumor occurrence or recurrence, or as therapy to arrest tumor growth or eradicate existence tumors or to prolong the survival.

ADMINISTRATION - The vaccine composition is administered by intradermal, subcutaneous or intravenous routes. Dosages range from 1 microg/kg-1 mg/kg, preferably 5-200 microg/kg.

ADVANTAGE - The method overcomes immunological tolerance which exists and represents a potential barrier to effectively vaccinating against human self tumor antigens, by immunizing an individual with a protein or peptide that is foreign (i.e., not identical to that in the individual) but nevertheless homologous to an individuals self tumor antigen or its portion. (26 pages)

L2 ANSWER 18 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:417000 CAPLUS
DN 135:32745
TI Antigen-binding fragments specific for tumor associated antigens
IN Dan, Michael; Entwistle, Joycelyn; Fast, Darren; Kaplan, Howard; Lewis, Keith; MacDonald, Glen; Maiti, Pradip
PA Novopharm Biotech Inc., Can.
SO PCT Int. Appl., 176 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001040292	A1	20010607	WO 1999-CA1141	19991129
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRAI WO 1999-CA1141 19991129

AB The present invention relates to antigen-binding fragments that are specific for stress protein-peptide complexes specifically associated with tumors, particularly human tumors, and compns. thereof. The compns. are suitable for diagnostic and pharmaceutical use. The invention further provides methods of making and screening for the antigen-binding fragments. The invention further encompasses compns. containing **cancer**-associated stress protein-peptide complexes (including derivs. thereof) and methods of use thereof. The **cancer**-specific stress protein-peptide complexes (SPPC's) are particularly useful in eliciting **cancer**-specific immunogenic responses against a plurality of **cancers**. The invention also provides novel phage display libraries for use in producing further SPPCs and anti-SPPCs of the invention.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 19 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2001:224352 CAPLUS

DN 134:251211

TI Monoclonal antibody to C-antigen: Prophylaxis and detection of **cancer**

IN Dan, Michael D.; Maiti, Pradip K.; Kaplan, Howard A.

PA Viventia Biotech, Inc., Can.

SO U.S., 56 pp., Cont.-in-part of U.S. Ser. No. 657,449, abandoned.
CODEN: USXXAM

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6207153	B1	20010327	US 1997-862124	19970522
	CA 2255540	AA	19971127	CA 1997-2255540	19970522
	CN 1229436	A	19990922	CN 1997-194815	19970522
	NZ 505305	A	20020628	NZ 1997-505305	19970522
	KR 2000015893	A	20000315	KR 1998-709444	19981121
	AU 775448	B2	20040729	AU 2000-72432	20001220
	US 2003021779	A1	20030130	US 2001-782397	20010213
	US 2004091484	A1	20040513	US 2003-651453	20030829
PRAI	US 1996-657449	B2	19960522		
	AU 1997-33696	A3	19970522		
	NZ 1997-332566	A1	19970522		
	US 1997-862124	A1	19970522		
	US 2001-782397	B1	20010213		

AB The authors disclose preparation and sequence characterization of monoclonal antibody H11 that specifically binds to an antigen (termed "C-antigen") expressed by diverse tumors and tumor cell lines. The C-antigen was not found on normal cells. Also disclosed are polynucleotides and single chain antibodies based on H11 for application in therapy and tumor imaging.

RE.CNT 124 THERE ARE 124 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 20 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2004:869162 CAPLUS
 DN 142:233296
 TI Consensus peptide presenting entities, screening methods, and use for the treatment and diagnosis of tumors.
 IN Maiti, Pradip K.; Herman, William; Dan, Michael D.; Kaplan, Howard A.; MacDonald, Glen C.; Entwistle, Jocelyn M.; Lewis, Keith E.; Fast, Darren G.
 PA Novopharm Biotech Inc., Can.
 SO Can. Pat. Appl., 155 pp.
 CODEN: CPXXEB
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	---	-----	-----	-----
PI	CA 2290722	AA	20010608	CA 1999-2290722	19991208
PRAI	CA 1999-2290722		19991208		

AB The invention provides antigen-binding-fragments specific for tumor cells and effective in treatment and/or diagnosing tumors. Methods of use are also provided as are methods for screening for addnl. such antigen-binding-fragments and the products obtained thereby.

L2 ANSWER 21 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3
 AN 2000:445203 CAPLUS
 DN 133:87934
 TI Priming tissue-specific cellular immunity in a phase I trial of autologous dendritic cells for prostate **cancer**
 AU Burch, Patrick A.; Breen, Jami K.; Buckner, Jan C.; Gastineau, Dennis A.; Kaur, Judith A.; Laus, Reiner L.; Padley, Douglas J.; Peshwa, Madhusudan V.; Pitot, Henry C.; Richardson, Ronald L.; Smits, Bouwien J.; Sopapan, Pitsata; Strang, George; Valone, Frank H.; Vuk-Pavlovic, Stanimir
 CS Divisions of Medical Oncology, Mayo Clinic and Mayo Foundation, Rochester, MN, 55905, USA
 SO Clinical Cancer Research (2000), 6(6), 2175-2182
 CODEN: CCREP4; ISSN: 1078-0432
 PB American Association for Cancer Research
 DT Journal
 LA English
 AB We attempted to induce therapeutic immunity against prostate-derived tissues in patients suffering from progressive hormone-refractory metastatic prostate carcinoma. Thirteen patients were treated with two infusions, 1 mo apart, of autologous dendritic cells (APC8015) preexposed ex vivo to PA2024, a fusion protein consisting of human granulocyte/macrophage-colony stimulating factor (GM-CSF

) and human prostatic acid phosphatase (PAP). The infusions were followed by three s.c. monthly doses of PA2024 without cells. Three groups of patients each received PA2024 at 0.3, 0.6, or 1.0 mg/injection. All Ps were two-sided. Treatment was well tolerated. After infusions of APC8015, patients experienced only mild (grade 1-2) short-lived fever and/or chills, myalgia, pain, and fatigue. One patient developed grade 3 fatigue. Four patients developed mild local reactions to s.c. PA2024. Twelve patients were evaluable for response to treatment. Circulating prostate-specific antigen levels dropped in three patients. T cells, drawn from patients after infusions of APC8015, but not before, could be stimulated in vitro by GM-CSF (P = 0.0004) and PAP (P = 0.0001), demonstrating broken immune tolerance against these two normal proteins. Injections of PA2024 did not influence the reactivity of T cells against PAP and GM-CSF. However, antibodies to GM-CSF and, to a much lesser extent, to PAP reached maximum titers only after two or even three injections of PA2024, showing that directly injected PA2024 was involved in stimulation of humoral immunity. Dendritic cells exposed to antigen ex

vivo can induce antigen-specific cellular immunity in prostate cancer patients, warranting further studies of this mode of immunotherapy.

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 22 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:444894 CAPLUS
DN 134:84982
TI PSA is a candidate self-antigen in autoimmune chronic prostatitis/chronic pelvic pain syndrome
AU Ponniah, Sathibalan; Arah, Ifeyinwa; Alexander, Richard B.
CS Division of Urology, University of Maryland School of Medicine, Baltimore, MD, USA
SO Prostate (New York) (2000), 44(1), 49-54
CODEN: PRSTDS; ISSN: 0270-4137
PB Wiley-Liss, Inc.
DT Journal
LA English
AB BACKGROUND. Previous studies demonstrated that recognition of seminal plasma antigens can occur in patients with chronic prostatitis/chronic pelvic pain syndrome. This suggests that an autoimmune component may contribute to symptoms in some men. To determine if any of the principal secretory proteins of the prostate could be candidate antigens in auto-immune prostatitis, we examined the recall proliferative response of purified CD4 T cells in patients with chronic prostatitis and in normal volunteers using purified seminal plasma antigens and autologous dendritic cells. METHODS. Peripheral blood mononuclear cells were harvested from 14 patients with chronic prostatitis and 12 normal volunteers by d. gradient centrifugation. The stimulating cells were irradiated autologous dendritic cells produced by culture of monocyte-enriched fractions with IL-4 and Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF). Purified CD4 T cells were the responding population. Recall proliferation assays were performed, using purified seminal plasma proteins as antigens. RESULTS. In 14 patients with chronic prostatitis, we detected a greater than 2-fold increase in proliferative response to PSA compared to control in 5 patients (36%). No response to Prostatic Acid Phosphatase (PAP) or β -microseminoprotein was observed in these 14 patients. In 12 normal volunteer donors with no history of genitourinary disease or symptoms, no proliferative response above background was observed for any prostatic antigen. CONCLUSIONS. The data suggest that some men with symptoms of chronic prostatitis have evidence of a proliferative CD4 T-cell response to PSA. PSA is a candidate antigen in chronic prostatitis/chronic pelvic pain syndrome and may be an appropriate target for immunotherapy for prostatic cancer.

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 23 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1998:661515 CAPLUS
DN 129:274703
TI Immunotherapy of B-cell malignancies using anti-CD22 antibodies
IN Goldenberg, David M.
PA IMMUNOMEDICS, INC., USA
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	---	-----	-----	-----
PI	WO 9842378	A1	19981001	WO 1998-US5075	19980317
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP,				

KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO,
 NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA,
 UG, US, UZ, VN, YU, ZW
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,
 FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,
 GA, GN, ML, MR, NE, SN, TD, TG

US 6183744	B1	20010206	US 1998-38955	19980312
CA 2284829	AA	19981001	CA 1998-2284829	19980317
AU 9867610	A1	19981020	AU 1998-67610	19980317
AU 728325	B2	20010104		
EP 969866	A1	20000112	EP 1998-912936	19980317
EP 969866	B1	20050615		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI

JP 2001518930	T2	20011016	JP 1998-545761	19980317
EP 1431311	A1	20040623	EP 2004-75775	19980317

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI

EP 1459768	A2	20040922	EP 2004-75774	19980317
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI

AT 297759	E	20050715	AT 1998-912936	19980317
ES 2241129	T3	20051016	ES 1998-912936	19980317
IN 189313	A	20030208	IN 1998-DE705	19980320
ZA 9802438	A	19981104	ZA 1998-2438	19980323

PRAI US 1997-41506P	P	19970324		
EP 1998-912936	A3	19980317		
WO 1998-US5075	W	19980317		

AB B-Cell malignancies, such as the B-cell subtype of non-Hodgkin's lymphoma and chronic lymphocytic leukemia, are significant contributors to **cancer** mortality. The response of B-cell malignancies to various forms of treatment is mixed. Traditional methods of treating B-cell malignancies, including chemotherapy and radiotherapy, have limited utility due to toxic side effects. Immunotherapy with anti-CD20 antibodies have also provided limited success. The use of antibodies that bind with the CD22 antigen, however, provides an effective means to treat B-cell malignancies such as indolent and aggressive forms of B-cell lymphomas, and acute and chronic forms of lymphatic leukemias. Moreover, immunotherapy with anti-CD22 antibodies requires comparatively low doses of antibody protein, and can be used effectively in multimodal therapies. Immunoconjugates comprising anti-CD22 antibody and radioisotope or cytokine, and combination treatment with chemotherapeutic agent are also disclosed.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 24 OF 25 BIOTECHNO COPYRIGHT 2006 Elsevier Science B.V. on STN
 DUPLICATE
 AN 1998:28369021 BIOTECHNO
 TI Defective expression of granulocyte-macrophage colony-stimulating
 factor/interleukin-3/interleukin-5 receptor common β chain in
 children with acute myeloid leukemia associated with respiratory failure
 AU Dirksen U.; Hattenhorst U.; Schneider P.; Schroten H.; Gobel U.; Bocking
 A.; Muller K.-M.; Murray R.; Burdach S.
 CS Dr. U. Dirksen, Pediatric Hematology/Oncology Dept., Children's Hospital
 Medical Center, 14.82 Moorenstr. 5, D-40225 Duesseldorf, Germany.
 E-mail: dirksen@uni-duesseldorf.de
 SO Blood, (15 AUG 1998), 92/4 (1097-1103), 35 reference(s)
 CODEN: BLOOAW ISSN: 0006-4971
 DT Journal; Article
 CY United States
 LA English
 SL English
 AB Deficiency of the granulocyte-macrophage colony-stimulating factor (

GM-CSF)/interleukin-3 (IL-3)/IL-5 receptors common β chain (β c) is a cause of fatal respiratory failure. β c deficiency manifests as pulmonary alveolar proteinosis (PAP). PAP has heterogeneous etiologies that may be genetic or acquired. Some cases of PAP have been reported to be associated with hematologic malignancies such as acute myeloid leukemia (AML). In mice, the PAP phenotype was generated by targeted deletion of the gene for β c and can be treated by transplantation of wild-type bone marrow into β c -/- mice. Thus, our findings in β c -/- mice provide evidence for a causal relationship between the lung disease and the hematopoietic system. We describe here expression defects of β c or β c plus GM-CSF receptor α chain (GM-CSFR α) in 3 pediatric patients with AML and PAP symptoms. All of the patients' leukemic cells failed to express normal levels of β c. The leukemic cells of patients number 2 and 3 additionally lacked the expression of GM-CSFR α , as shown by flow cytometry. Strikingly reduced or absent function of β c was demonstrated in clonogenic progenitor assays with absent colony-forming unit (CFU) growth after GM-CSF or IL-3 stimulation. The response to growth factors acting via a growth factor receptor distinct from the GM-CSF/IL-3/IL-5 system (recombinant human granulocyte colony-stimulating factor (rhG-CSF)) was normal. After antileukemic treatment, the pulmonary symptoms resolved and β c or β c plus GM-CSFR α expression was normal. Our findings provide evidence that a defect in the expression of β c or β c plus GM-CSFR α on AML blasts can be associated with respiratory failure in patients with AML.

L2 ANSWER 25 OF 25 Elsevier BIOBASE COPYRIGHT 2006 Elsevier Science B.V.
on STN
AN 1997107060 ESBIOBASE
TI Effects of Phytolacca acinosa polysaccharides I with different schedules
on its antitumor efficiency in tumor bearing mice and production of IL-1,
IL-2, IL-6, TNF, CSF activity in normal mice
AU Wang H.-B.; Zheng Q.-W.
CS H.-B. Wang, Department of Pharmacology, College of Pharmacy, Second
Military Medical University, Shanghai 200433, China.
SO Immunopharmacology and Immunotoxicology, (1997), 19/2 (197-213), 29
reference(s)
CODEN: IITOFI ISSN: 0892-3973
DT Journal; Article
CY United States
LA English
SL English
AB Effects of Phytolacca acinosa polysaccharides I (PAP-I), 5-40
mg/kg in timing of 7 times/wk, 3 times/wk and 1 time/wk on their
antitumor efficiency in Sarcoma-180 bearing mice were comparatively
investigated. The results confirmed that PAP-I (10 mg/kg, 3
times/wk) reached its optimal antitumor efficiency. Concanavalin A-,
lipopolysaccharides-induced lymphocyte proliferation and the IL-2
production were tested in normal mice which were treated with PAP
-I, 5-50 mg/kg in timing of 1 time/wk and 3 times/wk. The results showed
that PAP-I could augment lymphocyte proliferation and IL-2
production in the group treated with PAP-I in timing of once a
week. However, in the group 3 times/wk, PAP-I could
significantly weaken lymphocyte proliferation and IL-2 production.
Further studies on IL-1, TNF and IL-6 secreted from macrophages and the
level of CSF activity in serum of normal mice with different schedules
showed that PAP-I (10 mg/kg, 3 times/wk) was the best one in
regulating the production of IL-1, TNF, IL-6 and CSF activity. M-CSF was
confirmed in the serum by using monoclonal antibody of IL-3, GM
-CSF and polyclonal antibody of M-CSF. These results suggested
that the antitumor effect of PAP-I, may be mainly related to
its augmenting effect on macrophages in mice.

=> d his

(FILE 'HOME' ENTERED AT 11:57:08 ON 21 JUN 2006)

FILE 'CAPLUS, BIOENG, BIOTECHNO, BIOTECHDS, ESBIODASE' ENTERED AT
11:57:29 ON 21 JUN 2006

L1	31 S (PAP AND (GM (W) CSF) AND CANCER)
L2	25 DUPLICATE REMOVE L1 (6 DUPLICATES REMOVED)
L3	17 S (L2 AND PROSTATE)
L4	17 DUPLICATE REMOVE L3 (0 DUPLICATES REMOVED)

Welcome to DialogClassic Web(tm)

Dialog level 05.11.05D

Last logoff: 19jun06 10:05:08

Logon file001 21jun06 10:38:25

*** ANNOUNCEMENTS ***

NEW FILES RELEASED

***Trademarkscan - South Korea (File 655)

***Regulatory Affairs Journals (File 183)

***Index Chemicus (File 302)

***Inspec (File 202)

RESUMED UPDATING

***File 141, Reader's Guide Abstracts

RELOADS COMPLETED

***File 516, D&B--Dun's Market Identifiers

***File 523, D&B European Dun's Market Identifiers

***File 531, American Business Directory

*** MEDLINE has been reloaded with the 2006 MeSH (Files 154 & 155)

*** The 2005 reload of the CLAIMS files (Files 340, 341, 942)

is now available online.

DATABASES REMOVED

***File 196, FINDEX

***File 468, Public Opinion Online (POLL)

Chemical Structure Searching now available in Prous Science Drug

Data Report (F452), Prous Science Drugs of the Future (F453),

IMS R&D Focus (F445/955), Pharmaprojects (F128/928), Beilstein

Facts (F390), Derwent Chemistry Resource (F355) and Index Chemicus

(File 302).

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>>>and events, please visit What's New from Dialog at <<<

>>><http://www.dialog.com/whatsnew/>. You can find news about<<<

>>>a specific database by entering HELP NEWS <file number>.<<<

* * *

File 1:ERIC 1966-2006/May

(c) format only 2006 Dialog

Set Items Description

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Cost is in DialUnits

?

155, 159, 10, 203, 35, 5, 467, 73, 434, 34

>>>Unrecognizable Command

?

B 155, 159, 10, 203, 35, 5, 467, 73, 434, 34

21jun06 10:39:42 User290558 Session D54.1

\$1.12 0.321 DialUnits File1

\$1.12 Estimated cost File1

\$0.53 INTERNET

\$1.65 Estimated cost this search

\$1.65 Estimated total session cost 0.321 DialUnits

SYSTEM:OS - DIALOG OneSearch

File 155:MEDLINE(R) 1951-2006/Jun 20

(c) format only 2006 Dialog

***File 155: Please see HELP NEWS 154**

for information about recent updates added to MEDLINE.

File 159:Cancerlit 1975-2002/Oct

(c) format only 2002 Dialog

***File 159: Cancerlit is no longer updating.**

Please see HELP NEWS159.

File 10:AGRICOLA 70-2006/May

(c) format only 2006 Dialog

File 203:AGRIS 1974-2006/Mar

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File 35:Dissertation Abs Online 1861-2006/May

(c) 2006 ProQuest Info&Learning

File 5:Biosis Previews(R) 1969-2006/Jun W2

(c) 2006 The Thomson Corporation

File 467:ExtraMED(tm) 2000/Dec

(c) 2001 Informania Ltd.

***File 467: F467 will close on February 1, 2006.**

7.

File 73:EMBASE 1974-2006/Jun 21

(c) 2006 Elsevier Science B.V.

File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec

(c) 1998 Inst for Sci Info

File 34:SciSearch(R) Cited Ref Sci 1990-2006/Jun W3

(c) 2006 Inst for Sci Info

Set	Items	Description
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?

S (PSA AND (GM (W) CSF) AND PROSTATE)

54958 PSA

137699 GM

234248 CSF

60986 GM(W)CSF

345249 PROSTATE

S1 137 (PSA AND (GM (W) CSF) AND PROSTATE)

?

RD S1

S2 65 RD S1 (unique items)

?

Set	Items	Description
S1	137	(PSA AND (GM (W) CSF) AND PROSTATE)
S2	65	RD S1 (unique items)

?

S (PAP AND (GM (W) CSF) AND PROSTATE)

38783 PAP

137699 GM

234248 CSF

60986 GM(W)CSF

345249 PROSTATE

S3 28 (PAP AND (GM (W) CSF) AND PROSTATE)

?

RD S3

S4 11 RD S3 (unique items)

?

TYPE S4/FULL/1-11

4/9/1 (Item 1 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

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20889595 PMID: 16752945

Sipuleucel-T: APC 8015, APC-8015, Prostate Cancer Vaccine - Dendreon.

Drugs in R&D (New Zealand) 2006, 7 (3) p197-201, ISSN 1174-5886--

Print Journal Code: 100883647

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: In Data Review

Subfile: INDEX MEDICUS

Sipuleucel-T [APC 8015, Provenge((R))] is an autologous, dendritic cell-based vaccine under development with Dendreon Corporation for the treatment of androgen-independent and androgen-dependent prostate cancer. It was generated using the company's active immunotherapy platform to stimulate a patient's own immune system to specifically target and destroy cancer cells, while leaving healthy cells unharmed. This approach could provide patients with a meaningful survival benefit and an improved tolerability profile over existing anticancer therapies. Sipuleucel-T selectively targets the prostate-specific antigen (PSA) known as prostatic acid phosphatase (PAP) that is expressed in approximate, equals 95% of prostate cancers. It is produced by ex vivo exposure of dendritic cell precursors to PA 2024, a recombinant fusion protein composed of the PAP target fused to granulocyte-macrophage colony-stimulating factor (GM-CSF) and incorporated into Dendreon's proprietary Antigen Delivery Cassette trademark. Patients are typically administered three intravenous (IV)-infusions of the vaccine over a 1-month period as a complete course of therapy. It is undergoing late-stage clinical evaluation among patients with early and advanced prostate cancer. In November 2003, Kirin Brewery returned to Dendreon the full rights to Sipuleucel-T for Asia. In exchange, Dendreon licensed patent rights relating to the use of certain HLA-DR antibodies to Kirin for \$US20 million. This amended agreement enables Dendreon to complete ongoing discussions for a worldwide marketing and sales partnership for Sipuleucel-T. Similarly, Kirin is able to develop its HLA-DR monoclonal antibodies free of potential infringement claims arising from Dendreon's patent rights to HLA-DR. The licensing agreement relates to patent rights owned by Dendreon relating to monoclonal antibodies against the HLA-DR antigen. In addition, Dendreon retains rights to develop and commercialise its two existing HLA-DR monoclonal antibodies, DN 1921 and DN 1924, as well as other HLA-DR antibodies not being developed by Kirin. Previously, in May 1999, Dendreon and Kirin established a collaboration for the development of dendritic cell-based immunotherapeutics for cancer, including Sipuleucel-T. Under the agreement, Kirin would provide financial support for Dendreon's research on dendritic cells focused on developing immunotherapies for cancers most prevalent in Asia. Dendreon would retain US rights to products arising from the collaboration while Kirin would hold the rights to such immunotherapeutics in Asia and Oceania. In August 2005, Dendreon signed an agreement to lease a commercial manufacturing facility in Hanover, New Jersey, USA. The company intends to develop the facility to meet anticipated clinical and commercial demands of Sipuleucel-T as well as other active immunotherapy product candidates. Dendreon and Diosynth Biotechnology (Akzo Nobel) have an agreement for the commercial production of the PA 2024 antigen component of Sipuleucel-T. In November 2003,

Dendreon announced that Diosynth successfully manufactured PA 2024 on a commercial scale. In October 2001, Dendreon announced that Gambro Healthcare Inc. would provide a network of centres for cell collection to support commercial production and clinical development of various Dendreon vaccines, including Sipuleucel-T. Dendreon has outsourced its cell processing operations in Mountain View, California, USA to Progenitor Cell Therapy under an amended agreement signed in August 2002. This agreement is an expansion of an existing agreement, under which Progenitor provided Dendreon with cell-processing services through its facility in Hackensack, New Jersey, USA. The pivotal, two-stage, phase III trial (D9902 study) has been initiated at clinical sites in the US. The first stage of the trial (D9902A study) is a double-blind, placebo-controlled phase III trial designed to evaluate Sipuleucel-T in men with asymptomatic, metastatic, androgen-independent prostate cancer. The trial was originally designed to be the companion study to a previously completed phase III trial, called D9901. However, the D9902A study with 98 patients recruited was halted in December 2002, when analysis of the D9901 study revealed no statistically significant benefit in time to disease progression in the overall group, although a benefit was seen in a subgroup of patients with Gleason scores of ≤ 7 . In April 2002, the US FDA requested clarification regarding cellular composition of Sipuleucel-T and the suspension of additional patient enrolment for the D9902 study; the request was related solely to manufacturing issues without patient safety being an issue. Trial enrolment resumed in October 2002 following FDA authorisation. Dendreon amended the protocol for the D9902 study and is only recruiting patients with asymptomatic, metastatic, androgen-independent prostate cancer, regardless of their Gleason Score (D9902B study). The ongoing pivotal phase I

Record Date Created: 20060606

4/9/2 (Item 2 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

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19998843 PMID: 16115700

Safety and immunological efficacy of a prostate cancer plasmid DNA vaccine encoding prostatic acid phosphatase (PAP).

Johnson Laura E; Frye Thomas P; Arnot Alana R; Marquette Carrie; Couture Larry A; Gendron-Fitzpatrick Annette; McNeel Douglas G

Department of Medicine, Section of Medical Oncology, University of Wisconsin-Madison, K4/518 Clinical Science Center, 600 Highland Avenue, Madison, WI 53792, USA.

Vaccine (Netherlands) Jan 16 2006, 24 (3) p293-303, ISSN 0264-410X
--Print Journal Code: 8406899

Contract/Grant No.: K23 RR16489; RR; NCRR

Publishing Model Print-Electronic

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS; Toxbib

Prostatic acid phosphatase (PAP) is a prostate tumor antigen currently being investigated as a target antigen in several human vaccine trials, some with evidence of clinical benefit. We have previously demonstrated that plasmid DNA vaccines encoding either human or rat PAP can elicit antigen-specific cellular and humoral immunity in rat models. The current study was performed to determine the safety and potential immunological efficacy in rodents of large and repetitive doses of a GMP-grade plasmid DNA vaccine encoding human PAP, pTVG-HP. Fifty-four male Lewis rats were immunized intradermally at 2-week intervals with 100, 500, or 1,500 microg

pTVG-HP with 5 microg recombinant rat GM-CSF protein given as a vaccine adjuvant. An additional 12 male Lewis rats served as controls with groups immunized with 1,500 microg of a parental DNA vector not encoding human PAP, and a group that received GM-CSF protein only without plasmid DNA. Groups of animals (n=3-6) were euthanized after two, four, or six immunizations with collections of tissues and blood for toxicity assessment and immunological analysis. No significant toxicities were observed in terms of animal weights, histopathology, hematological changes, or changes in serum chemistries. Six of fifty-four were found to have subtle evidence of possible renal toxicity; however these findings were not statistically different from control animals. The vaccine was found to be effective in eliciting PAP-specific CD4 and CD8 T cells, predominantly Th1 in type, in all immunized animals at all doses and numbers of immunizations. PAP-specific IgG were detected in a dose-dependent fashion, with titers increasing after multiple immunizations. These studies demonstrate that, in rats, immunization with the pTVG-HP vaccine is safe and effective in eliciting PAP-specific cellular and humoral immune responses. These findings support the further clinical evaluation of pTVG-HP in patients with prostate cancer.

Tags: Male

Descriptors: *Acid Phosphatase--immunology--IM; *Cancer Vaccines--immunology--IM; *Prostate--enzymology--EN; *Prostate--immunology--IM; *Prostatic Neoplasms--immunology--IM; *Prostatic Neoplasms--prevention and control--PC; Animals; Antibody Formation--immunology--IM; Cancer Vaccines--adverse effects--AE; Cancer Vaccines--toxicity--TO; Enzyme-Linked Immunosorbent Assay; Immunity, Cellular--immunology--IM; Immunoglobulin G--biosynthesis--BI; Immunoglobulin G--immunology--IM; Plasmids--immunology--IM; Rats; Rats, Inbred Lew; Research Support, N.I.H., Extramural; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, Non-P.H.S.; Spleen--immunology--IM; T-Lymphocytes--immunology--IM; Vaccines, DNA--adverse effects--AE; Vaccines, DNA--immunology--IM; Vaccines, DNA--toxicity--TO

CAS Registry No.: 0 (Cancer Vaccines); 0 (Immunoglobulin G); 0 (Plasmids); 0 (Vaccines, DNA)

Enzyme No.: EC 3.1.3.2 (Acid Phosphatase)

Record Date Created: 20051219

Record Date Completed: 20060227

Date of Electronic Publication: 20050809

4/9/3 (Item 3 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

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14916534 PMID: 15176049

Immunotherapy (APC8015, Provenge) targeting prostatic acid phosphatase can induce durable remission of metastatic androgen-independent prostate cancer: a Phase 2 trial.

Burch Patrick A; Croghan Gary A; Gastineau Dennis A; Jones Lori A; Kaur Judith S; Kylstra Jelle W; Richardson Ronald L; Valone Frank H; Vuk-Pavlovic Stanimir

Division of Medical Oncology, Department of Oncology, Mayo Clinic, Rochester, Minnesota 55902, USA.

Prostate (United States) Aug 1 2004, 60 (3) p197-204, ISSN 0270-4137--Print Journal Code: 8101368

Publishing Model Print

Document type: Clinical Trial; Clinical Trial, Phase II; Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS; Toxbib

BACKGROUND: Prostate cancer is the most commonly diagnosed malignancy in American men, yet treatment of its metastatic androgen-independent form remains inadequate. This mandates development of new therapies such as immunotherapy. In this Phase 2 trial, we determined the efficacy of antigen presenting cells (APCs) loaded with PA2024, a recombinant fusion protein containing prostatic acid phosphatase (PAP) and GM-CSF. **METHODS:** We enrolled 21 patients with histologically documented androgen-independent prostate carcinoma that could be evaluated by radionuclide bone scan or computed tomography scan. APC8015 was prepared from a leukapheresis product; it contained autologous CD54-positive PA2024-loaded APCs with admixtures of monocytes, macrophages, B and T cells. APC8015 was infused intravenously twice, 2 weeks apart. Two weeks after the second infusion, patients received three subcutaneous injections of 1.0 mg of PA2024 1 month apart. We monitored patients' physical condition, immune response, and laboratory parameters. **RESULTS:** Nineteen patients could be evaluated for response to treatment. The median time to progression was 118 days. Treatment was tolerated reasonably well; most adverse effects were secondary to APC8015 and were NCI Common Toxicity Criteria Grade 1-2. Four of the 21 patients reported Grade 3-4 adverse events. Two patients exhibited a transient 25-50% decrease in prostate-specific antigen (PSA). For a third patient, PSA dropped from 221 ng/ml at baseline to undetectable levels by week 24 and has remained so for more than 4 years. In addition, this patient's metastatic retroperitoneal and pelvic adenopathy has resolved. PBMC collected from patients for at least 16 weeks proliferated upon in vitro stimulation by PA2024. For the patient with responsive disease, PBMC could be stimulated for 96 weeks. **CONCLUSIONS:** This study demonstrates a definite clinical response of androgen-independent prostate cancer to APC immunotherapy. Currently we are studying this mode of therapy in Phase 3 trials. Copyright 2004 Wiley-Liss, Inc.

Tags: Male

Descriptors: *Antigen-Presenting Cells--immunology--IM; *Carcinoma--immunology--IM; *Carcinoma--therapy--TH; *Immunotherapy--methods--MT; *Prostatic Neoplasms--immunology--IM; *Prostatic Neoplasms--therapy--TH; *Protein-Tyrosine-Phosphatase--genetics--GE; Aged; Aged, 80 and over; Carcinoma--pathology--PA; Granulocyte-Macrophage Colony-Stimulating Factor--administration and dosage--AD; Granulocyte-Macrophage Colony-Stimulating Factor--genetics--GE; Granulocyte-Macrophage Colony-Stimulating Factor--pharmacology--PD; Humans; Infusions, Intravenous; Injections, Subcutaneous; Middle Aged; Neoplasm Metastasis; Prostate-Specific Antigen--analysis--AN; Prostatic Neoplasms--pathology--PA; Protein-Tyrosine-Phosphatase--administration and dosage--AD; Protein-Tyrosine-Phosphatase--pharmacology--PD; Recombinant Fusion Proteins; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, Non-P.H.S.; Treatment Outcome

CAS Registry No.: 0 (Recombinant Fusion Proteins); 83869-56-1 (Granulocyte-Macrophage Colony-Stimulating Factor)

Enzyme No.: EC 3.1.3.- (prostatic acid phosphatase); EC 3.1.3.48 (Protein-Tyrosine-Phosphatase); EC 3.4.21.77 (Prostate-Specific Antigen)

Record Date Created: 20040603

Record Date Completed: 20040903

4/9/4 (Item 4 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

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14576452 PMID: 14609763

[Cell therapy and prostate cancer]

Therapie cellulaire et cancer de la prostate.

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Unite fonctionnelle de recherche clinique et de therapie cellulaire,
 Institut Jean-Godinot, 1. av du general Koenig, 51056 Reims, France.
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Bulletin du cancer (France) Aug-Sep 2003, 90 (8-9) p734-43, ISSN
 0007-4551--Print Journal Code: 0072416

Publishing Model Print

Document type: Journal Article; Review ; English Abstract

Languages: FRENCH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Hormonotherapy is the standard treatment for advanced prostate cancer but disease progression ineluctably occurs. Subsequent chemotherapy has a modest symptomatic palliative role even if encouraging results were recently presented with docetaxel and estramustine combination. In this context, there is a great deal of interest in using dendritic cells therapeutically, as they are the most potent professional antigen-presenting cells in the immune system. Based on their unique adjuvant capacity, two vaccinal strategies are therefore tested in clinical trials. First approach includes the administration of cancer cells transduced by a cytokine gene to stimulate the in vivo recruitment and activation of dendritic cells, and the most advanced studies use GM-CSF gene-transduced allogenic cells. The second approach consists in infusions of dendritic cells loaded ex vivo with relevant tumoral antigens. Two prostate antigens have already been used. PSMA evaluated in 130 patients and a fusion protein PAP-GM-CSF (Provence) in 144 patients. All treatments were well tolerated and frequently generated weak specific responses, but resulted in a limited clinical efficacy. However, engineering of dendritic cells can provide optimised cell vectors able to amplify vaccine response and clinical efficacy. John Libbey Eurotext 2003 (63 Refs.)

Tags: Male

Descriptors: *Dendritic Cells--transplantation--TR; *Immunotherapy
 --methods--MT; *Prostate-Specific Antigen--immunology--IM; *Prostatic
 Neoplasms--therapy--TH; Acid Phosphatase--immunology--IM; Antigen-Presentin
 g Cells--immunology--IM; Antigen-Presenting Cells--transplantation--TR;
 Antigens, Surface--immunology--IM; Cancer Vaccines--immunology--IM; Cell
 Movement; Clinical Trials, Phase I; Dendritic Cells--immunology--IM;
 English Abstract; Glutamate Carboxypeptidase II--immunology--IM;
 Granulocyte-Macrophage Colony-Stimulating Factor--immunology--IM; Humans;
 Immunity, Cellular; Major Histocompatibility Complex--immunology--IM;
 Prostate--enzymology--EN; Prostatic Neoplasms--immunology--IM; Recombinant
 Fusion Proteins--immunology--IM

CAS Registry No.: 0 (Antigens, Surface); 0 (Cancer Vaccines); 0
 (Recombinant Fusion Proteins); 83869-56-1 (Granulocyte-Macrophage
 Colony-Stimulating Factor)

Enzyme No.: EC 3.1.3.2 (Acid Phosphatase); EC 3.4.17.21 (Glutamate
 Carboxypeptidase II); EC 3.4.17.21 (glutamate carboxypeptidase II, human)
 ; EC 3.4.21.77 (Prostate-Specific Antigen)

Record Date Created: 20031111

Record Date Completed: 20031204

4/9/5 (Item 5 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

12763307 PMID: 10873066

Priming tissue-specific cellular immunity in a phase I trial of
 autologous dendritic cells for prostate cancer.

Burch P A; Breen J K; Buckner J C; Gastineau D A; Kaur J A; Laus R L;

Padley D J; Peshwa M V; Pitot H C; Richardson R L; Smits B J; Sopapan P; Strang G; Valone F H; Vuk-Pavlovic S

Division of Medical Oncology, Mayo Clinic and Mayo Foundation, Rochester, Minnesota 55905, USA.

Clinical cancer research - an official journal of the American Association for Cancer Research (UNITED STATES) Jun 2000, 6 (6) p2175-82, ISSN 1078-0432--Print Journal Code: 9502500

Publishing Model Print

Document type: Clinical Trial; Clinical Trial, Phase I; Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

We attempted to induce therapeutic immunity against prostate-derived tissues in patients suffering from progressive hormone-refractory metastatic prostate carcinoma. Thirteen patients were treated with two infusions, 1 month apart, of autologous dendritic cells (APC8015) preexposed ex vivo to PA2024, a fusion protein consisting of human granulocyte/macrophage-colony stimulating factor (GM-CSF) and human prostatic acid phosphatase (PAP). The infusions were followed by three s.c. monthly doses of PA2024 without cells. Three groups of patients each received PA2024 at 0.3, 0.6, or 1.0 mg/injection. All Ps were two-sided. Treatment was well tolerated. After infusions of APC8015, patients experienced only mild (grade 1-2) short-lived fever and/or chills, myalgia, pain, and fatigue. One patient developed grade 3 fatigue. Four patients developed mild local reactions to s.c. PA2024. Twelve patients were evaluable for response to treatment. Circulating prostate-specific antigen levels dropped in three patients. T cells, drawn from patients after infusions of APC8015, but not before, could be stimulated in vitro by GM-CSF ($P = 0.0004$) and PAP ($P = 0.0001$), demonstrating broken immune tolerance against these two normal proteins. Injections of PA2024 did not influence the reactivity of T cells against PAP and GM-CSF. However, antibodies to GM-CSF and, to a much lesser extent, to PAP reached maximum titers only after two or even three injections of PA2024, showing that directly injected PA2024 was involved in stimulation of humoral immunity. Dendritic cells exposed to antigen ex vivo can induce antigen-specific cellular immunity in prostate cancer patients, warranting further studies of this mode of immunotherapy.

Tags: Male

Descriptors: *Acid Phosphatase--therapeutic use--TU; *Dendritic Cells--immunology--IM; *Granulocyte-Macrophage Colony-Stimulating Factor--therapeutic use--TU; *Immunotherapy--methods--MT; *Prostatic Neoplasms--immunology--IM; *Prostatic Neoplasms--therapy--TH; *Recombinant Fusion Proteins--therapeutic use--TU; Acid Phosphatase--blood--BL; Antigen-Presenting Cells--immunology--IM; Cell Division--immunology--IM; Dose-Response Relationship, Drug; Humans; Injections, Subcutaneous; Prostate; Research Support, Non-U.S. Gov't; T-Lymphocytes--drug effects--DE; T-Lymphocytes--immunology--IM; Time Factors; Transplantation, Autologous

CAS Registry No.: 0 (Recombinant Fusion Proteins); 83869-56-1 (Granulocyte-Macrophage Colony-Stimulating Factor)

Enzyme No.: EC 3.1.3.2 (Acid Phosphatase); EC 3.1.3.2 (PA2024 fusion protein, human)

Record Date Created: 20000929

Record Date Completed: 20001207

4/9/6 (Item 6 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

12756334 PMID: 10861757

PSA is a candidate self-antigen in autoimmune chronic prostatitis/chronic pelvic pain syndrome.

Ponniah S; Arah I; Alexander R B

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21201, USA. sponniah@smail.umaryland.edu

Prostate (UNITED STATES) Jun 15 2000, 44 (1) p49-54, ISSN 0270-4137

--Print Journal Code: 8101368

Contract/Grant No.: R01-DK53732; DK; NIDDK

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

BACKGROUND: Previous studies demonstrated that recognition of seminal plasma antigens can occur in patients with chronic prostatitis/chronic pelvic pain syndrome. This suggests that an autoimmune component may contribute to symptoms in some men. To determine if any of the principal secretory proteins of the prostate could be candidate antigens in autoimmune prostatitis, we examined the recall proliferative response of purified CD4 T cells in patients with chronic prostatitis and in normal volunteers using purified seminal plasma antigens and autologous dendritic cells. **METHODS:** Peripheral blood mononuclear cells were harvested from 14 patients with chronic prostatitis and 12 normal volunteers by density gradient centrifugation. The stimulating cells were irradiated autologous dendritic cells produced by culture of monocyte-enriched fractions with IL-4 and Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF). Purified CD4 T cells were the responding population. Recall proliferation assays were performed, using purified seminal plasma proteins as antigens. **RESULTS:** In 14 patients with chronic prostatitis, we detected a greater than 2-fold increase in proliferative response to PSA compared to control in 5 patients (36%). No response to Prostatic Acid Phosphatase (PAP) or beta-microseminoprotein was observed in these 14 patients. In 12 normal volunteer donors with no history of genitourinary disease or symptoms, no proliferative response above background was observed for any prostatic antigen. **CONCLUSIONS:** The data suggest that some men with symptoms of chronic prostatitis have evidence of a proliferative CD4 T-cell response to PSA. PSA is a candidate antigen in chronic prostatitis/chronic pelvic pain syndrome and may be an appropriate target for immunotherapy for prostatic cancer. Copyright 2000 Wiley-Liss, Inc.

Tags: Male

Descriptors: *Autoimmune Diseases--immunology--IM; *Pelvic Pain
--immunology--IM; *Prostate-Specific Antigen--immunology--IM; *Prostatitis
--immunology--IM; Adult; Aged; CD4-Positive T-Lymphocytes--immunology--IM;
Cell Division; Centrifugation, Density Gradient; Chronic Disease; Dendritic
Cells--immunology--IM; Flow Cytometry; Granulocyte-Macrophage
Colony-Stimulating Factor--immunology--IM; Humans; Immunomagnetic
Separation; Interleukin-4--immunology--IM; Microspheres; Middle Aged;
Research Support, U.S. Gov't, Non-P.H.S.; Research Support, U.S. Gov't,
P.H.S.; Scintillation Counting; Syndrome

CAS Registry No.: 207137-56-2 (Interleukin-4); 83869-56-1
(Granulocyte-Macrophage Colony-Stimulating Factor)

Enzyme No.: EC 3.4.21.77 (Prostate-Specific Antigen)

Record Date Created: 20000710

Record Date Completed: 20000710

4/9/7 (Item 1 from file: 159)

DIALOG(R)File 159:Cancerlit

(c) format only 2002 Dialog. All rts. reserv.

02600878 PMID: 99701197

Immunotherapy of Hormone Refractory Prostate Cancer (HRPC) with Prostatic Acid Phosphatase (PAP)-Loaded Dendritic Cells (APC8015) (Meeting abstract).

Valone; Small; Peshwa; Strang; Laus; Ruegg; Schooten W va
University of California, San Francisco, San Francisco, CA.

Proc Annu Meet Am Soc Clin Oncol 1999, 18,

Document Type: MEETING ABSTRACTS

Languages: ENGLISH

Main Citation Owner: NOTNLM

Record type: Completed

Dendritic cells (DC) are the most potent natural antigen presenting cells (APC) for stimulating immune responses. Twenty-eight men with HRPC were enrolled in a Phase I/II trial of APC8015, prepared and infused intravenously monthly for 3 months. To prepare APC8015, DC precursors are isolated from peripheral leukapheresis products by buoyant density centrifugation and then incubated for 40 hours in serum-free, cytokine-free media with PA2024, which is a fusion protein composed of PAP and a DC targeting element, structurally similar to GM-CSF. Twelve men were treated in a phase I trial of escalating doses of APC8015 (0.2 to 1.2×10^6 nucleated cells/m²) and 16 were enrolled in a phase II trial at the maximum dose. Median age was 69 (range: 48-83). Median ECOG performance was 0 (range: 0-1). Median PSA was 63 ng/ml (range: 3.4-1,007). <10% of infusions were associated with mild fevers or myalgias. There were no other treatment-related adverse events. APC8015 induced strong T cell responses to PA2024 in all patients but induced specific antibodies in <20% of patients. IFN- γ but not IL-4 was detected by ELISPOT and ELISA assays suggesting a TH-1 response to PA2024. Antigen-specific T cell precursor frequencies were $<1/10^5$ before treatment and as high as $1/5,000$ after treatment. 2 of 22 evaluable patients had >50% decrease in PSA and 4 had a 25-49% decrease (6 too early). Median time to disease progression was 43 weeks in the phase II trial. PAP-loaded DC are safe and effective for stimulating antigen-specific immune responses. Initial phase II data suggest that treatment is clinically active. (C) American Society of Clinical Oncology 1999.

Record Date Created: 19991001

4/9/8 (Item 1 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0015804453 BIOSIS NO.: 200600149848

Provenge (R) - Prostate cancer therapy

AUTHOR: McIntyre J A (Reprint); Fernandez D

AUTHOR ADDRESS: Prous Sci, POB 540, Barcelona 08080, Spain**Spain

JOURNAL: Drugs of the Future 30 (9): p892-895 SEP 2005 2005

ISSN: 0377-8282

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: There are few therapeutic options available for the treatment of hormone-refractory prostate cancer (HRPC), but recent advancements in the understanding of immune recognition have resulted in the development of novel vaccine products aimed at inducing prostate-specific T-cell-mediated immunity. Provenge((R)) (APC-8015) is an

immunotherapeutic consisting of autologous dendritic cell precursors loaded ex vivo with a recombinant fusion protein (PA2024) comprising prostatic acid phosphatase (PAP), an antigen found in 95% of prostate cancers, and granulocyte-macrophage colony-stimulating factor (GM-CSF). Early clinical studies demonstrated good tolerability of the product and T-cell proliferation responses to PA2024. Phase II studies indicated the preliminary efficacy of Provenge((R)), with increases in prostate-specific antigen (PSA) doubling time and PSA-modulating effects. Subsequent placebo-controlled phase III studies identified advantages for Provenge in terms of time to disease progression and time to onset of disease-related pain.

REGISTRY NUMBERS: 83869-56-1: granulocyte-macrophage colony-stimulating factor; 9001-77-8: prostatic acid phosphatase

ENZYME COMMISSION NUMBER: EC 3.4.21.77: prostate-specific antigen; EC 3.1.3.2: prostatic acid phosphatase

DESCRIPTORS:

MAJOR CONCEPTS: Pharmacology; Clinical Immunology--Human Medicine, Medical Sciences; Oncology--Human Medicine, Medical Sciences

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGANISMS: human (Hominidae)

ORGANISMS: PARTS ETC: T-cell--immune system, blood and lymphatics

COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates

DISEASES: hormone refractory prostate cancer {HRPC}--neoplastic disease, reproductive system disease/male, drug therapy

MESH TERMS: Prostatic Neoplasms (MeSH)

CHEMICALS & BIOCHEMICALS: prostate-specific antigen {PSA}; vaccines--immunologic-drug, immunostimulant-drug, vaccine; granulocyte-macrophage colony-stimulating factor {GM-CSF}; prostatic acid phosphatase {PAP}; PA2024 fusion protein; provenge--antineoplastic-drug, immunologic-drug, phase II clinical trial

CONCEPT CODES:

02506 Cytology - Animal

02508 Cytology - Human

10064 Biochemistry studies - Proteins, peptides and amino acids

12512 Pathology - Therapy

15002 Blood - Blood and lymph studies

15004 Blood - Blood cell studies

16506 Reproductive system - Pathology

17002 Endocrine - General

22002 Pharmacology - General

22005 Pharmacology - Clinical pharmacology

22018 Pharmacology - Immunological processes and allergy

24003 Neoplasms - Immunology

24004 Neoplasms - Pathology, clinical aspects and systemic effects

24008 Neoplasms - Therapeutic agents and therapy

34502 Immunology - General and methods

34508 Immunology - Immunopathology, tissue immunology

BIOSYSTEMATIC CODES:

86215 Hominidae

4/9/9 (Item 2 from file: 5)

DIALOG(R) File 5: Biosis Previews(R)

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0015000622 BIOSIS NO.: 200400371411

Immunotherapy (APC8015, Provenge(R)) targeting prostatic acid phosphatase

can induce durable remission of metastatic androgen-independent prostate cancer: A phase 2 trial

AUTHOR: Burch Patrick A; Croghan Gary A; Gastineau Dennis A; Jones Lori A; Kaur Judith S; Kylstra Jelle W; Richardson Ronald L; Valone Frank H; Vuk-Pavlovic Stanimir (Reprint)
AUTHOR ADDRESS: Dept OncolDiv Med Oncol, Mayo Clin, Guggenheim 901B, 200 1st St SW, Rochester, MN, 55902, USA**USA
AUTHOR E-MAIL ADDRESS: vuk@mayo.edu
JOURNAL: Prostate 60 (3): p197-204 August 1, 2004 2004
MEDIUM: print
ISSN: 0270-4137 (ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: BACKGROUND. Prostate cancer is the most commonly diagnosed malignancy in American men, yet treatment of its metastatic androgen-independent form remains inadequate. This mandates development of new therapies such as immunotherapy. In this Phase 2 trial, we determined the efficacy of antigen presenting cells (APCs) loaded with PA2024, a recombinant fusion protein containing prostatic acid phosphatase (PAP) and GM-CSF. METHODS. We enrolled 21 patients with histologically documented androgen-independent prostate carcinoma that could be evaluated by radionuclide bone scan or computed tomography scan. APC8015 was prepared from a leukapheresis product; it contained autologous CD54-positive PA2024-loaded APCs with admixtures of monocytes, macrophages, B and T cells. APC8015 was infused intravenously twice, 2 weeks apart. Two weeks after the second infusion, patients received three subcutaneous injections of 1.0 mg of PA2024 1 month apart. We monitored patients' physical condition, immune response, and laboratory parameters. RESULTS. Nineteen patients could be evaluated for response to treatment. The median time to progression was 118 days. Treatment was tolerated reasonably well; most adverse effects were secondary to APC8015 and were NCI Common Toxicity Criteria Grade 1-2. Four of the 21 patients reported Grade 3-4 adverse events. Two patients exhibited a transient 25-50% decrease in prostate-specific antigen (PSA). For a third patient, PSA dropped from 221 ng/ml at baseline to undetectable levels by week 24 and has remained so for more than 4 years. In addition, this patient's metastatic retroperitoneal and pelvic adenopathy has resolved. PBMC collected from patients for at least 16 weeks proliferated upon in vitro stimulation by PA2024. For the patient with responsive disease, PBMC could be stimulated for 96 weeks. CONCLUSIONS. This study demonstrates a definite clinical response of androgen-independent prostate cancer to APC immunotherapy. Currently we are studying this mode of therapy in Phase 3 trials. Copyright 2004 Wiley-Liss, Inc.

REGISTRY NUMBERS: 350229-75-3: Provenge; 83869-56-1: granulocyte-macrophage colony stimulating factor; 9001-77-8: prostatic acid phosphatase
ENZYME COMMISSION NUMBER: EC 3.4.21.77: prostate-specific antigen; EC 3.1.3.2: prostatic acid phosphatase

DESCRIPTORS:

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Clinical Immunology--Human Medicine, Medical Sciences; Oncology--Human Medicine, Medical Sciences; Pharmacology

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGANISMS: human (Hominidae)--male, American

ORGANISMS: PARTS ETC: B cell--blood and lymphatics, immune system; CD54 positive cell--immune system; T cell--blood and lymphatics, immune system; antigen-presenting cell--immune system, intravenous infusion;

macrophage--blood and lymphatics, immune system; monocyte--blood and lymphatics, immune system; peripheral blood mononuclear cell {PBMC}--blood and lymphatics, immune system

COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates

DISEASES: androgen-independent prostate cancer--neoplastic disease, reproductive system disease/male, urologic disease, therapy; metastatic retroperitoneal adenopathy--disease-miscellaneous; pelvic adenopathy--disease-miscellaneous; prostate cancer--neoplastic disease, reproductive system disease/male, urologic disease, diagnosis, therapy

MESH TERMS: Prostatic Neoplasms (MeSH); Prostatic Neoplasms (MeSH)

CHEMICALS & BIOCHEMICALS: PA2024 fusion protein; Provenge {APC8015}--antineoplastic-drug, immunologic-drug, immunostimulant-drug, phase II clinical trial; granulocyte-macrophage colony stimulating factor {GM-CSF}; prostate-specific antigen; prostatic acid phosphatase

METHODS & EQUIPMENT: computed tomography scan--clinical techniques, diagnostic techniques, imaging and microscopy techniques, laboratory techniques; immunotherapy--clinical techniques, immunologic techniques, laboratory techniques, therapeutic and prophylactic techniques; radionuclide bone scan--clinical techniques, diagnostic techniques

MISCELLANEOUS TERMS: National Cancer Institute {NCI}; National Cancer Institute common toxicity criteria grade 1-4 {NCI common toxicity criteria grade 1-4}; immune response

CONCEPT CODES:

02506 Cytology - Animal
02508 Cytology - Human
10060 Biochemistry studies - General
10064 Biochemistry studies - Proteins, peptides and amino acids
12504 Pathology - Diagnostic
12512 Pathology - Therapy
15002 Blood - Blood and lymph studies
15004 Blood - Blood cell studies
15506 Urinary system - Pathology
16506 Reproductive system - Pathology
17002 Endocrine - General
22002 Pharmacology - General
22005 Pharmacology - Clinical pharmacology
22018 Pharmacology - Immunological processes and allergy
24001 Neoplasms - Diagnostic methods
24003 Neoplasms - Immunology
24004 Neoplasms - Pathology, clinical aspects and systemic effects
24008 Neoplasms - Therapeutic agents and therapy
34502 Immunology - General and methods
34508 Immunology - Immunopathology, tissue immunology

BIOSYSTEMATIC CODES:

86215 Hominidae

4/9/10 (Item 3 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0013557956 BIOSIS NO.: 200200151467

Stability characterization of antigen-loaded dendritic cell vaccines

AUTHOR: Nevin Barry (Reprint); Therond Judy; Ishisaka Toshiye (Reprint);

Shiomoto Clifford; Kothari Sudesh S (Reprint); Galie Brian; Yumiaco

Orlando Jr; Westerman Rick; Terral Annette; Peshwa Madhusudan V (Reprint)

AUTHOR ADDRESS: Cell Process Development, Dendreon, Seattle, WA, USA**USA

JOURNAL: Blood 98 (11 Part 2): p38b November 16, 2001 2001

MEDIUM: print

CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 2 Orlando, Florida, USA. December 07-11, 2001; 20011207
SPONSOR: American Society of Hematology
ISSN: 0006-4971
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: ProvengeTM, an immunotherapy product consisting of autologous dendritic cells (DC) loaded ex vivo with a recombinant engineered prostate tumor-antigen (PA2024) consisting of prostatic acid phosphatase (PAP) fused to granulocyte macrophage colony stimulating factor (GM-CSF), is currently in phase III clinical evaluation for treatment of hormone refractory prostate cancer. The patients leukapheresis product was shipped to Dendreon's cGMP cell processing centers where it was processed to enrich dendritic cells, incubated with PA2024 for 36-44 hours, then harvested and formulated in Lactated Ringer's solution for injection, USP and returned to the clinical site for administration. Stability studies were designed wherein the final DC vaccine product was stored refrigerated at 2-8°C and samples were analyzed at 0, 8, 12, 24, 30 and 36 hours post-formulation. Samples were characterized for nucleated cell number, cell viability, phenotype, potency, and allogeneic and autologous T cell stimulatory capacity. The dendritic cell fraction was characterized for expression of a variety of co-stimulatory molecules including CD1a, CD11c, CD40, CD54, CD80, CD83, CD86, CD123, HLA-DR, and HLA-A,B,C. Results indicate that there is no difference in any of the product characteristics between 0 and 8 hours. Beyond 8 hours there was no difference in cell viability and phenotype over the stability period evaluated. There was approximately a 10-20% decrease in cell number, potency and T cell stimulatory capacity over a course of 36 hours. The implications of the observed in vitro results on in vivo potency will be discussed.

REGISTRY NUMBERS: 350229-75-3: Provenge; 83869-56-1: granulocyte macrophage colony stimulating factor

DESCRIPTORS:

MAJOR CONCEPTS: Clinical Immunology--Human Medicine, Medical Sciences; Oncology--Human Medicine, Medical Sciences; Pharmacology
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae)--patient
ORGANISMS: PARTS, ETC: T cell--blood and lymphatics, immune system; dendritic cells--immune system
COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates
DISEASES: prostate cancer--neoplastic disease, reproductive system disease/male, urologic disease
MESH TERMS: Prostatic Neoplasms (MeSH)
CHEMICALS & BIOCHEMICALS: Provenge--antineoplastic-drug, immunologic-drug, stability, vaccine; granulocyte macrophage colony stimulating factor; prostate tumor-antigen; prostatic acid phosphatase
MISCELLANEOUS TERMS: Meeting Abstract; Meeting Abstract

CONCEPT CODES:

00520 General biology - Symposia, transactions and proceedings
02506 Cytology - Animal
02508 Cytology - Human
12512 Pathology - Therapy
15002 Blood - Blood and lymph studies
15004 Blood - Blood cell studies
15506 Urinary system - Pathology

16506 Reproductive system - Pathology
 22002 Pharmacology - General
 22005 Pharmacology - Clinical pharmacology
 22018 Pharmacology - Immunological processes and allergy
 24003 Neoplasms - Immunology
 24004 Neoplasms - Pathology, clinical aspects and systemic effects
 24008 Neoplasms - Therapeutic agents and therapy
 34502 Immunology - General and methods
 34508 Immunology - Immunopathology, tissue immunology
 BIOSYSTEMATIC CODES:
 86215 Hominidae

4/9/11 (Item 1 from file: 73)
 DIALOG(R)File 73:EMBASE
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13316952 EMBASE No: 2005387607

Session II: Tumor antigens - Prostate cancer antigens and vaccines

Salgaller M.L.; Elgamal A.-A.; Bosch M.; Lodge A.; Shankar G.; Boynton A.
 ; Belldegrun A.; Logothetis C.; Papandreou C.

Dr. M.L. Salgaller, Northwest Biotherapeutics, Inc., Seattle, WA United States

Cancer Immunology, Immunotherapy (CANCER IMMUNOL. IMMUNOTHER.) (Germany)
) 2003, 52/SUPPL. 1 (S8-S9+S27)

CODEN: CIIMD ISSN: 0340-7004

DOCUMENT TYPE: Journal ; Conference Paper

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The clinical development of prostate cancer vaccines presents several challenges. Reagents are more limited and difficult to obtain as compared with other tumor types. The advanced age of the patient population presents the researcher with subjects having diminished immune systems and who are often less willing to undergo procedures for research purposes. Consequently, the majority of research has involved those cancers for which tumor and immune cells are readily available. Despite these hurdles, new and novel approaches are improving the poor overall survival rates through the development of antigen-based treatment options. These efforts are particularly important in the realm of hormone-refractory prostate cancer (HRPC), since no therapy exists with significant clinical impact. This is a major issue for the 36,000 men who will die from the disease annually, despite transient responses to secondary treatment such as hormone ablation therapy. During the past few years, candidate target antigens for experimental vaccines have been identified in several laboratories. These include oncogenes, overexpressed proteins, and carbohydrates. Three of the furthest in clinical development are well-established clinical markers of prostate cancer: prostate-specific membrane antigen (PSMA), prostate-specific antigen (PSA), and prostatic acid phosphatase (PAP). Following conclusive preclinical evidence indicating that the human body responds immunologically to prostate antigens, clinical trials have been underway for many years with PSMA, PSA, and PAP as targets. We investigated the capacity of a vaccine composed of autologous dendritic cells (DC), pulsed ex vivo with recombinant PSMA (rPS-MA), to safely generate clinically meaningful antitumor immune responses in HRPC patients. In 2000 and 2001, 32 patients with metastatic or non-metastatic HRPC were enrolled in a phase I/II clinical trial. Their peripheral blood mononuclear cells were isolated by leukapheresis, matured to DC by in vitro culture with maturation factors (GM-CSF, IL-4, and inactivated BCG) for up to 7 days, followed by rPSMA loading and harvesting of the vaccine. Patients received four intradermal treatments of 5, 10, or 20-million rPSMA-loaded mature DC

at monthly intervals, followed by up to a total of 6 months of observation. Measurement of serum anti-PSMA antibodies, PSMA-stimulated lymphocyte proliferation, and delayed-type hypersensitivity (DTH) skin testing were carried out before, during, and after vaccination. Clinical responses were assessed by CT/bone scans and hematochemical laboratory tests, including PSA levels. More than 140 total vaccine injections were well tolerated; no clinical signs of autoimmunity or serious adverse events were observed. Overall, 54% of patients achieved stability of their disease at >6 months follow-up, as assessed by radiographic criteria, and 83% of patients had a PSMA-specific immune response, 92% of patients with stable disease had a PSMA-specific immune response, and 46% of patients had a decrease in PSA velocity. Compared to baseline, 93% of 27 evaluable patients converted to DTH-positive against the BCG component of the vaccine. Due to these promising initial findings we have initiated a double-blind, placebo-controlled phase III clinical trial. (c) 2002 Northwest Biotherapeutics, Inc. All rights reserved.

DRUG DESCRIPTORS:

*tumor antigen; *cancer vaccine--adverse drug reaction--ae; *cancer vaccine--clinical trial--ct; *cancer vaccine--drug therapy--dt
 tumor rejection antigen; tumor suppressor protein; prostate antigen; acid phosphatase prostate isoenzyme; prostate specific antigen; prostate specific membrane antigen--drug therapy--dt; prostate specific membrane antigen--intradermal drug administration--dl; prostate specific membrane antigen--pharmacology--pd; recombinant antigen--drug therapy--dt; recombinant antigen--intradermal drug administration--dl; recombinant antigen--pharmacology--pd; dendritic cell vaccine--adverse drug reaction--ae; dendritic cell vaccine--clinical trial--ct; dendritic cell vaccine--drug therapy--dt

MEDICAL DESCRIPTORS:

*prostate cancer--drug therapy--dt
 prostatectomy; cancer surgery; bone metastasis; cancer cell culture; T lymphocyte; medical research; cancer chemotherapy; immune response; cancer survival; quality of life; dendritic cell; peripheral blood mononuclear cell; skin irritation--side effect--si; injection site reaction--side effect--si; headache--side effect--si; fatigue--side effect--si; human; clinical trial; conference paper; priority journal

SECTION HEADINGS:

- 016 Cancer
- 026 Immunology, Serology and Transplantation
- 028 Urology and Nephrology
- 037 Drug Literature Index
- 038 Adverse Reaction Titles

?

Set	Items	Description
S1	137	(PSA AND (GM (W) CSF) AND PROSTATE)
S2	65	RD S1 (unique items)
S3	28	(PAP AND (GM (W) CSF) AND PROSTATE)
S4	11	RD S3 (unique items)

?

Set	Items	Description
S1	137	(PSA AND (GM (W) CSF) AND PROSTATE)
S2	65	RD S1 (unique items)
S3	28	(PAP AND (GM (W) CSF) AND PROSTATE)
S4	11	RD S3 (unique items)

?

S (PAP AND (GM (W) CSF) AND CANCER)

38783 PAP
137699 GM
234248 CSF
60986 GM(W)CSF
3460920 CANCER

S5 35 (PAP AND (GM (W) CSF) AND CANCER)

?

RD S5

S6 18 RD S5 (unique items)

?

TYPE S6/FULL/1-18

6/9/1 (Item 1 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

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20889595 PMID: 16752945

Sipuleucel-T: APC 8015, APC-8015, Prostate Cancer Vaccine - Dendreon.

Drugs in R&D (New Zealand) 2006, 7 (3) p197-201, ISSN 1174-5886--
Print Journal Code: 100883647
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Data Review
Subfile: INDEX MEDICUS

Sipuleucel-T [APC 8015, Provenge((R))] is an autologous, dendritic cell-based vaccine under development with Dendreon Corporation for the treatment of androgen-independent and androgen-dependent prostate cancer. It was generated using the company's active immunotherapy platform to stimulate a patient's own immune system to specifically target and destroy cancer cells, while leaving healthy cells unharmed. This approach could provide patients with a meaningful survival benefit and an improved tolerability profile over existing anticancer therapies. Sipuleucel-T selectively targets the prostate-specific antigen (PSA) known as prostatic acid phosphatase (PAP) that is expressed in approximate, equals 95% of prostate cancers. It is produced by ex vivo exposure of dendritic cell precursors to PA 2024, a recombinant fusion protein composed of the PAP target fused to granulocyte-macrophage colony-stimulating factor (GM-CSF) and incorporated into Dendreon's proprietary Antigen Delivery Cassette trademark. Patients are typically administered three intravenous (IV)-infusions of the vaccine over a 1-month period as a complete course of therapy. It is undergoing late-stage clinical evaluation among patients with early and advanced prostate cancer. In November 2003, Kirin Brewery returned to Dendreon the full rights to Sipuleucel-T for Asia. In exchange, Dendreon licensed patent rights relating to the use of certain HLA-DR antibodies to Kirin for \$US20 million. This amended agreement enables Dendreon to complete ongoing discussions for a worldwide marketing and sales partnership for Sipuleucel-T. Similarly, Kirin is able to develop its HLA-DR monoclonal antibodies free of potential infringement claims arising from Dendreon's patent rights to HLA-DR. The licensing agreement relates to patent rights owned by Dendreon relating to monoclonal antibodies against the HLA-DR antigen. In addition, Dendreon retains rights to develop and commercialise its two existing HLA-DR monoclonal antibodies, DN 1921 and DN 1924, as well as other HLA-DR antibodies not being developed by Kirin. Previously, in May 1999, Dendreon and Kirin established a

collaboration for the development of dendritic cell-based immunotherapeutics for cancer, including Sipuleucel-T. Under the agreement, Kirin would provide financial support for Dendreon's research on dendritic cells focused on developing immunotherapies for cancers most prevalent in Asia. Dendreon would retain US rights to products arising from the collaboration while Kirin would hold the rights to such immunotherapeutics in Asia and Oceania. In August 2005, Dendreon signed an agreement to lease a commercial manufacturing facility in Hanover, New Jersey, USA. The company intends to develop the facility to meet anticipated clinical and commercial demands of Sipuleucel-T as well as other active immunotherapy product candidates. Dendreon and Diosynth Biotechnology (Akzo Nobel) have an agreement for the commercial production of the PA 2024 antigen component of Sipuleucel-T. In November 2003, Dendreon announced that Diosynth successfully manufactured PA 2024 on a commercial scale. In October 2001, Dendreon announced that Gambro Healthcare Inc. would provide a network of centres for cell collection to support commercial production and clinical development of various Dendreon vaccines, including Sipuleucel-T. Dendreon has outsourced its cell processing operations in Mountain View, California, USA to Progenitor Cell Therapy under an amended agreement signed in August 2002. This agreement is an expansion of an existing agreement, under which Progenitor provided Dendreon with cell-processing services through its facility in Hackensack, New Jersey, USA. The pivotal, two-stage, phase III trial (D9902 study) has been initiated at clinical sites in the US. The first stage of the trial (D9902A study) is a double-blind, placebo-controlled phase III trial designed to evaluate Sipuleucel-T in men with asymptomatic, metastatic, androgen-independent prostate cancer. The trial was originally designed to be the companion study to a previously completed phase III trial, called D9901. However, the D9902A study with 98 patients recruited was halted in December 2002, when analysis of the D9901 study revealed no statistically significant benefit in time to disease progression in the overall group, although a benefit was seen in a subgroup of patients with Gleason scores of ≤ 7 . In April 2002, the US FDA requested clarification regarding cellular composition of Sipuleucel-T and the suspension of additional patient enrolment for the D9902 study; the request was related solely to manufacturing issues without patient safety being an issue. Trial enrolment resumed in October 2002 following FDA authorisation. Dendreon amended the protocol for the D9902 study and is only recruiting patients with asymptomatic, metastatic, androgen-independent prostate cancer, regardless of their Gleason Score (D9902B study). The ongoing pivotal phase I

Record Date Created: 20060606

6/9/2 (Item 2 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

19998843 PMID: 16115700

Safety and immunological efficacy of a prostate cancer plasmid DNA vaccine encoding prostatic acid phosphatase (PAP).

Johnson Laura E; Frye Thomas P; Arnot Alana R; Marquette Carrie; Couture Larry A; Gendron-Fitzpatrick Annette; McNeel Douglas G

Department of Medicine, Section of Medical Oncology, University of Wisconsin-Madison, K4/518 Clinical Science Center, 600 Highland Avenue, Madison, WI 53792, USA.

Vaccine (Netherlands). Jan 16 2006, 24 (3) p293-303, ISSN 0264-410X
--Print Journal Code: 8406899

Contract/Grant No.: K23 RR16489; RR; NCRR

Publishing Model Print-Electronic

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS; Toxibib

Prostatic acid phosphatase (PAP) is a prostate tumor antigen currently being investigated as a target antigen in several human vaccine trials, some with evidence of clinical benefit. We have previously demonstrated that plasmid DNA vaccines encoding either human or rat PAP can elicit antigen-specific cellular and humoral immunity in rat models. The current study was performed to determine the safety and potential immunological efficacy in rodents of large and repetitive doses of a GMP-grade plasmid DNA vaccine encoding human PAP, pTVG-HP. Fifty-four male Lewis rats were immunized intradermally at 2-week intervals with 100, 500, or 1,500 microg pTVG-HP with 5 microg recombinant rat GM-CSF protein given as a vaccine adjuvant. An additional 12 male Lewis rats served as controls with groups immunized with 1,500 microg of a parental DNA vector not encoding human PAP, and a group that received GM-CSF protein only without plasmid DNA. Groups of animals (n=3-6) were euthanized after two, four, or six immunizations with collections of tissues and blood for toxicity assessment and immunological analysis. No significant toxicities were observed in terms of animal weights, histopathology, hematological changes, or changes in serum chemistries. Six of fifty-four were found to have subtle evidence of possible renal toxicity, however these findings were not statistically different from control animals. The vaccine was found to be effective in eliciting PAP-specific CD4 and CD8 T cells, predominantly Th1 in type, in all immunized animals at all doses and numbers of immunizations. PAP-specific IgG were detected in a dose-dependent fashion, with titers increasing after multiple immunizations. These studies demonstrate that, in rats, immunization with the pTVG-HP vaccine is safe and effective in eliciting PAP-specific cellular and humoral immune responses. These findings support the further clinical evaluation of pTVG-HP in patients with prostate cancer.

Tags: Male

Descriptors: *Acid Phosphatase--immunology--IM; *Cancer Vaccines--immunology--IM; *Prostate--enzymology--EN; *Prostate--immunology--IM; *Prostatic Neoplasms--immunology--IM; *Prostatic Neoplasms--prevention and control--PC; Animals; Antibody Formation--immunology--IM; Cancer Vaccines--adverse effects--AE; Cancer Vaccines--toxicity--TO; Enzyme-Linked Immunosorbent Assay; Immunity, Cellular--immunology--IM; Immunoglobulin G--biosynthesis--BI; Immunoglobulin G--immunology--IM; Plasmids--immunology--IM; Rats; Rats, Inbred Lew; Research Support, N.I.H., Extramural; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, Non-P.H.S.; Spleen--immunology--IM; T-Lymphocytes--immunology--IM; Vaccines, DNA--adverse effects--AE; Vaccines, DNA--immunology--IM; Vaccines, DNA--toxicity--TO

CAS Registry No.: 0 (Cancer Vaccines); 0 (Immunoglobulin G); 0 (Plasmids); 0 (Vaccines, DNA)

Enzyme No.: EC 3.1.3.2 (Acid Phosphatase)

Record Date Created: 20051219

Record Date Completed: 20060227

Date of Electronic Publication: 20050809

6/9/3 (Item 3 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

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14916534 PMID: 15176049

Immunotherapy (APC8015, Provenge) targeting prostatic acid phosphatase can induce durable remission of metastatic androgen-independent prostate

cancer: a Phase 2 trial.

Burch Patrick A; Croghan Gary A; Gastineau Dennis A; Jones Lori A; Kaur Judith S; Kylstra Jelle W; Richardson Ronald L; Valone Frank H; Vuk-Pavlovic Stanimir

Division of Medical Oncology, Department of Oncology, Mayo Clinic, Rochester, Minnesota 55902, USA.

Prostate (United States) Aug 1 2004, 60 (3) p197-204, ISSN 0270-4137--Print Journal Code: 8101368

Publishing Model Print

Document type: Clinical Trial; Clinical Trial, Phase II; Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS; Toxbib

BACKGROUND: Prostate cancer is the most commonly diagnosed malignancy in American men, yet treatment of its metastatic androgen-independent form remains inadequate. This mandates development of new therapies such as immunotherapy. In this Phase 2 trial, we determined the efficacy of antigen presenting cells (APCs) loaded with PA2024, a recombinant fusion protein containing prostatic acid phosphatase (PAP) and GM-CSF. **METHODS:** We enrolled 21 patients with histologically documented androgen-independent prostate carcinoma that could be evaluated by radionuclide bone scan or computed tomography scan. APC8015 was prepared from a leukapheresis product; it contained autologous CD54-positive PA2024-loaded APCs with admixtures of monocytes, macrophages, B and T cells. APC8015 was infused intravenously twice, 2 weeks apart. Two weeks after the second infusion, patients received three subcutaneous injections of 1.0 mg of PA2024 1 month apart. We monitored patients' physical condition, immune response, and laboratory parameters. **RESULTS:** Nineteen patients could be evaluated for response to treatment. The median time to progression was 118 days. Treatment was tolerated reasonably well; most adverse effects were secondary to APC8015 and were NCI Common Toxicity Criteria Grade 1-2. Four of the 21 patients reported Grade 3-4 adverse events. Two patients exhibited a transient 25-50% decrease in prostate-specific antigen (PSA). For a third patient, PSA dropped from 221 ng/ml at baseline to undetectable levels by week 24 and has remained so for more than 4 years. In addition, this patient's metastatic retroperitoneal and pelvic adenopathy has resolved. PBMC collected from patients for at least 16 weeks proliferated upon in vitro stimulation by PA2024. For the patient with responsive disease, PBMC could be stimulated for 96 weeks. **CONCLUSIONS:** This study demonstrates a definite clinical response of androgen-independent prostate cancer to APC immunotherapy. Currently we are studying this mode of therapy in Phase 3 trials. Copyright 2004 Wiley-Liss, Inc.

Tags: Male

Descriptors: *Antigen-Presenting Cells--immunology--IM; *Carcinoma--immunology--IM; *Carcinoma--therapy--TH; *Immunotherapy--methods--MT; *Prostatic Neoplasms--immunology--IM; *Prostatic Neoplasms--therapy--TH; *Protein-Tyrosine-Phosphatase--genetics--GE; Aged; Aged, 80 and over; Carcinoma--pathology--PA; Granulocyte-Macrophage Colony-Stimulating Factor--administration and dosage--AD; Granulocyte-Macrophage Colony-Stimulating Factor--genetics--GE; Granulocyte-Macrophage Colony-Stimulating Factor--pharmacology--PD; Humans; Infusions, Intravenous; Injections, Subcutaneous; Middle Aged; Neoplasm Metastasis; Prostate-Specific Antigen--analysis--AN; Prostatic Neoplasms--pathology--PA; Protein-Tyrosine-Phosphatase--administration and dosage--AD; Protein-Tyrosine-Phosphatase--pharmacology--PD; Recombinant Fusion Proteins; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, Non-P.H.S.; Treatment Outcome

CAS Registry No.: 0 (Recombinant Fusion Proteins); 83869-56-1 (Granulocyte-Macrophage Colony-Stimulating Factor)

Enzyme No.: EC 3.1.3.- (prostatic acid phosphatase); EC 3.1.3.48

(Protein-Tyrosine-Phosphatase); EC 3.4.21.77 (Prostate-Specific Antigen)
 Record Date Created: 20040603
 Record Date Completed: 20040903

6/9/4 (Item 4 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

14576452 PMID: 14609763

[Cell therapy and prostate cancer]

Therapie cellulaire et cancer de la prostate.

Eymard Jean-Christophe; Bernard J

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 Institut Jean-Godinot, 1. av du general Koenig, 51056 Reims, France.
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Bulletin du cancer (France) Aug-Sep 2003, 90 (8-9) p734-43, ISSN
 0007-4551--Print Journal Code: 0072416

Publishing Model Print

Document type: Journal Article; Review ; English Abstract

Languages: FRENCH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Hormonotherapy is the standard treatment for advanced prostate cancer but disease progression ineluctably occurs. Subsequent chemotherapy has a modest symptomatic palliative role even if encouraging results were recently presented with docetaxel and estramustine combination. In this context, there is a great deal of interest in using dendritic cells therapeutically, as they are the most potent professional antigen-presenting cells in the immune system. Based on their unique adjuvant capacity, two vaccinal strategies are therefore tested in clinical trials. First approach includes the administration of cancer cells transduced by a cytokine gene to stimulate the in vivo recruitment and activation of dendritic cells, and the most advanced studies use GM-CSF gene-transduced allogenic cells. The second approach consists in infusions of dendritic cells loaded ex vivo with relevant tumoral antigens. Two prostate antigens have already been used. PSMA evaluated in 130 patients and a fusion protein PAP-GM-CSF (Provenge) in 144 patients. All treatments were well tolerated and frequently generated weak specific responses, but resulted in a limited clinical efficacy. However, engineering of dendritic cells can provide optimised cell vectors able to amplify vaccine response and clinical efficacy. John Libbey Eurotext 2003 (63 Refs.)

Tags: Male

Descriptors: *Dendritic Cells--transplantation--TR; *Immunotherapy
 --methods--MT; *Prostate-Specific Antigen--immunology--IM; *Prostatic
 Neoplasms--therapy--TH; Acid Phosphatase--immunology--IM; Antigen-Presentin
 g Cells--immunology--IM; Antigen-Presenting Cells--transplantation--TR;
 Antigens, Surface--immunology--IM; Cancer Vaccines--immunology--IM; Cell
 Movement; Clinical Trials, Phase I; Dendritic Cells--immunology--IM;
 English Abstract; Glutamate Carboxypeptidase II--immunology--IM;
 Granulocyte-Macrophage Colony-Stimulating Factor--immunology--IM; Humans;
 Immunity, Cellular; Major Histocompatibility Complex--immunology--IM;
 Prostate--enzymology--EN; Prostatic Neoplasms--immunology--IM; Recombinant
 Fusion Proteins--immunology--IM

CAS Registry No.: 0 (Antigens, Surface); 0 (Cancer Vaccines); 0
 (Recombinant Fusion Proteins); 83869-56-1 (Granulocyte-Macrophage
 Colony-Stimulating Factor)

Enzyme No.: EC 3.1.3.2 (Acid Phosphatase); EC 3.4.17.21 (Glutamate
 Carboxypeptidase II); EC 3.4.17.21 (glutamate carboxypeptidase II, human)

; EC 3.4.21.77 (Prostate-Specific Antigen)
Record Date Created: 20031111
Record Date Completed: 20031204

6/9/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts.. reserv.

12763307 PMID: 10873066

Priming tissue-specific cellular immunity in a phase I trial of autologous dendritic cells for prostate cancer.

Burch P A; Breen J K; Buckner J C; Gastineau D A; Kaur J A; Laus R L; Padley D J; Peshwa M V; Pitot H C; Richardson R L; Smits B J; Sopapan P; Strang G; Valone F H; Vuk-Pavlovic S

Division of Medical Oncology, Mayo Clinic and Mayo Foundation, Rochester, Minnesota 55905, USA.

Clinical cancer research - an official journal of the American Association for Cancer Research (UNITED STATES) Jun 2000, 6 (6) p2175-82, ISSN 1078-0432--Print Journal Code: 9502500

Publishing Model Print

Document type: Clinical Trial; Clinical Trial, Phase I; Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

We attempted to induce therapeutic immunity against prostate-derived tissues in patients suffering from progressive hormone-refractory metastatic prostate carcinoma. Thirteen patients were treated with two infusions, 1 month apart, of autologous dendritic cells (APC8015) preexposed ex vivo to PA2024, a fusion protein consisting of human granulocyte/macrophage-colony stimulating factor (GM-CSF) and human prostatic acid phosphatase (PAP). The infusions were followed by three s.c. monthly doses of PA2024 without cells. Three groups of patients each received PA2024 at 0.3, 0.6, or 1.0 mg/injection. All Ps were two-sided. Treatment was well tolerated. After infusions of APC8015, patients experienced only mild (grade 1-2) short-lived fever and/or chills, myalgia, pain, and fatigue. One patient developed grade 3 fatigue. Four patients developed mild local reactions to s.c. PA2024. Twelve patients were evaluable for response to treatment. Circulating prostate-specific antigen levels dropped in three patients. T cells, drawn from patients after infusions of APC8015, but not before, could be stimulated in vitro by GM-CSF ($P = 0.0004$) and PAP ($P = 0.0001$), demonstrating broken immune tolerance against these two normal proteins. Injections of PA2024 did not influence the reactivity of T cells against PAP and GM-CSF. However, antibodies to GM-CSF and, to a much lesser extent, to PAP reached maximum titers only after two or even three injections of PA2024, showing that directly injected PA2024 was involved in stimulation of humoral immunity. Dendritic cells exposed to antigen ex vivo can induce antigen-specific cellular immunity in prostate cancer patients, warranting further studies of this mode of immunotherapy.

Tags: Male

Descriptors: *Acid Phosphatase--therapeutic use--TU; *Dendritic Cells--immunology--IM; *Granulocyte-Macrophage Colony-Stimulating Factor--therapeutic use--TU; *Immunotherapy--methods--MT; *Prostatic Neoplasms--immunology--IM; *Prostatic Neoplasms--therapy--TH; *Recombinant Fusion Proteins--therapeutic use--TU; Acid Phosphatase--blood--BL; Antigen-Presenting Cells--immunology--IM; Cell Division--immunology--IM; Dose-Response Relationship, Drug; Humans; Injections, Subcutaneous; Prostate; Research Support, Non-U.S. Gov't; T-Lymphocytes--drug effects--DE; T-Lymphocytes

--immunology--IM; Time Factors; Transplantation, Autologous
CAS Registry No.: 0 (Recombinant Fusion Proteins); 83869-56-1
(Granulocyte-Macrophage Colony-Stimulating Factor)
Enzyme No.: EC 3.1.3.2 (Acid Phosphatase); EC 3.1.3.2 (PA2024 fusion
protein, human)
Record Date Created: 20000929
Record Date Completed: 20001207

6/9/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

12756334 PMID: 10861757
PSA is a candidate self-antigen in autoimmune chronic prostatitis/chronic
pelvic pain syndrome.
Ponniah S; Arah I; Alexander R B
Division of Urology, University of Maryland School of Medicine, and
Section of Urology, VA Maryland Health Care System, Baltimore, Maryland
21201, USA. sponniah@smail.umaryland.edu
Prostate (UNITED STATES) Jun 15 2000, 44 (1) p49-54, ISSN 0270-4137
--Print Journal Code: 8101368
Contract/Grant No.: R01-DK53732; DK; NIDDK
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS

BACKGROUND: Previous studies demonstrated that recognition of seminal
plasma antigens can occur in patients with chronic prostatitis/chronic
pelvic pain syndrome. This suggests that an autoimmune component may
contribute to symptoms in some men. To determine if any of the principal
secretory proteins of the prostate could be candidate antigens in
autoimmune prostatitis, we examined the recall proliferative response of
purified CD4 T cells in patients with chronic prostatitis and in normal
volunteers using purified seminal plasma antigens and autologous dendritic
cells. METHODS: Peripheral blood mononuclear cells were harvested from 14
patients with chronic prostatitis and 12 normal volunteers by density
gradient centrifugation. The stimulating cells were irradiated autologous
dendritic cells produced by culture of monocyte-enriched fractions with
IL-4 and Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF).
Purified CD4 T cells were the responding population. Recall proliferation
assays were performed, using purified seminal plasma proteins as antigens.
RESULTS: In 14 patients with chronic prostatitis, we detected a greater
than 2-fold increase in proliferative response to PSA compared to control
in 5 patients (36%). No response to Prostatic Acid Phosphatase (PAP) or
beta-microseminoprotein was observed in these 14 patients. In 12 normal
volunteer donors with no history of genitourinary disease or symptoms, no
proliferative response above background was observed for any prostatic
antigen. CONCLUSIONS: The data suggest that some men with symptoms of
chronic prostatitis have evidence of a proliferative CD4 T-cell response to
PSA. PSA is a candidate antigen in chronic prostatitis/chronic pelvic pain
syndrome and may be an appropriate target for immunotherapy for prostatic
cancer. Copyright 2000 Wiley-Liss, Inc.

Tags: Male

Descriptors: *Autoimmune Diseases--immunology--IM; *Pelvic Pain
--immunology--IM; *Prostate-Specific Antigen--immunology--IM; *Prostatitis
--immunology--IM; Adult; Aged; CD4-Positive T-Lymphocytes--immunology--IM;
Cell Division; Centrifugation, Density Gradient; Chronic Disease; Dendritic

Cells--immunology--IM; Flow Cytometry; Granulocyte-Macrophage Colony-Stimulating Factor--immunology--IM; Humans; Immunomagnetic Separation; Interleukin-4--immunology--IM; Microspheres; Middle Aged; Research Support, U.S. Gov't, Non-P.H.S.; Research Support, U.S. Gov't, P.H.S.; Scintillation Counting; Syndrome
 CAS Registry No.: 207137-56-2 (Interleukin-4); 83869-56-1 (Granulocyte-Macrophage Colony-Stimulating Factor)
 Enzyme No.: EC 3.4.21.77 (Prostate-Specific Antigen)
 Record Date Created: 20000710
 Record Date Completed: 20000710

6/9/7 (Item 1 from file: 159)
 DIALOG(R) File 159: Cancerlit
 (c) format only 2002 Dialog. All rts. reserv.

02600878 PMID: 99701197
Immunotherapy of Hormone Refractory Prostate Cancer (HRPC) with Prostatic Acid Phosphatase (PAP)-Loaded Dendritic Cells (APC8015) (Meeting abstract).
 Valone; Small; Peshwa; Strang; Laus; Ruegg; Schooten W va
 University of California, San Francisco, San Francisco, CA.
 Proc Annu Meet Am Soc Clin Oncol 1999, 18,
 Document Type: MEETING ABSTRACTS
 Languages: ENGLISH
 Main Citation Owner: NOTNLM
 Record type: Completed

Dendritic cells (DC) are the most potent natural antigen presenting cells (APC) for stimulating immune responses. Twenty-eight men with HRPC were enrolled in a Phase I/II trial of APC8015, prepared and infused intravenously monthly for 3 months. To prepare APC8015, DC precursors are isolated from peripheral leukapheresis products by buoyant density centrifugation and then incubated for 40 hours in serum-free, cytokine-free media with PA2024, which is a fusion protein composed of PAP and a DC targeting element, structurally similar to GM-CSF. Twelve men were treated in a phase I trial of escalating doses of APC8015 (0.2 to 1.2 x 10⁹ nucleated cells/m²) and 16 were enrolled in a phase II trial at the maximum dose. Median age was 69 (range: 48-83). Median ECOG performance was 0 (range: 0-1). Median PSA was 63 ng/ml (range: 3.4-1,007). <10% of infusions were associated with mild fevers or myalgias. There were no other treatment-related adverse events. APC8015 induced strong T cell responses to PA2024 in all patients but induced specific antibodies in <20% of patients. IFN- γ but not IL-4 was detected by ELISPOT and ELISA assays suggesting a TH-1 response to PA2024. Antigen-specific T cell precursor frequencies were <1/10⁵ before treatment and as high as 1/5,000 after treatment. 2 of 22 evaluable patients had >50% decrease in PSA and 4 had a 25-49% decrease (6 too early). Median time to disease progression was 43 weeks in the phase II trial. PAP-loaded DC are safe and effective for stimulating antigen-specific immune responses. Initial phase II data suggest that treatment is clinically active. (C) American Society of Clinical Oncology 1999.

Record Date Created: 19991001

6/9/8 (Item 1 from file: 5)
 DIALOG(R) File 5: Biosis Previews(R)
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0015804453 BIOSIS NO.: 200600149848
 Provenge (R) - Prostate cancer therapy

AUTHOR: McIntyre J A (Reprint); Fernandez D
AUTHOR ADDRESS: Prous Sci, POB 540, Barcelona 08080, Spain**Spain
JOURNAL: Drugs of the Future 30 (9): p892-895 SEP 2005 2005
ISSN: 0377-8282
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: There are few therapeutic options available for the treatment of hormone-refractory prostate cancer (HRPC), but recent advancements in the understanding of immune recognition have resulted in the development of novel vaccine products aimed at inducing prostate-specific T-cell-mediated immunity. Provenge((R)) (APC-8015) is an immunotherapeutic consisting of autologous dendritic cell precursors loaded ex vivo with a recombinant fusion protein (PA2024) comprising prostatic acid phosphatase (PAP), an antigen found in 95% of prostate cancers, and granulocyte-macrophage colony-stimulating factor (GM-CSF). Early clinical studies demonstrated good tolerability of the product and T-cell proliferation responses to PA2024. Phase II studies indicated the preliminary efficacy of Provenge((R)), with increases in prostate-specific antigen (PSA) doubling time and PSA-modulating effects. Subsequent placebo-controlled phase III studies identified advantages for Provenge in terms of time to disease progression and time to onset of disease-related pain.

REGISTRY NUMBERS: 83869-56-1: granulocyte-macrophage colony-stimulating factor; 9001-77-8: prostatic acid phosphatase

ENZYME COMMISSION NUMBER: EC 3.4.21.77: prostate-specific antigen; EC 3.1.3.2: prostatic acid phosphatase

DESCRIPTORS:

MAJOR CONCEPTS: Pharmacology; Clinical Immunology--Human Medicine, Medical Sciences; Oncology--Human Medicine, Medical Sciences

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGANISMS: human (Hominidae)

ORGANISMS: PARTS ETC: T-cell--immune system, blood and lymphatics

COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates

DISEASES: hormone refractory prostate cancer {HRPC}--neoplastic disease, reproductive system disease/male, drug therapy

MESH TERMS: Prostatic Neoplasms (MeSH)

CHEMICALS & BIOCHEMICALS: prostate-specific antigen {PSA}; vaccines--immunologic-drug, immunostimulant-drug, vaccine; granulocyte-macrophage colony-stimulating factor {GM-CSF}; prostatic acid phosphatase {PAP}; PA2024 fusion protein; provenge--antineoplastic-drug, immunologic-drug, phase II clinical trial

CONCEPT CODES:

02506 Cytology - Animal

02508 Cytology - Human

10064 Biochemistry studies - Proteins, peptides and amino acids

12512 Pathology - Therapy

15002 Blood - Blood and lymph studies

15004 Blood - Blood cell studies

16506 Reproductive system - Pathology

17002 Endocrine - General

22002 Pharmacology - General

22005 Pharmacology - Clinical pharmacology

22018 Pharmacology - Immunological processes and allergy

24003 Neoplasms - Immunology

24004 Neoplasms - Pathology, clinical aspects and systemic effects

24008 Neoplasms - Therapeutic agents and therapy
34502 Immunology - General and methods
34508 Immunology - Immunopathology, tissue immunology

BIOSYSTEMATIC CODES:

86215 Hominidae

6/9/9 (Item 2 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0015000622 BIOSIS NO.: 200400371411

Immunotherapy (APC8015, Provenge(R)) targeting prostatic acid phosphatase can induce durable remission of metastatic androgen-independent prostate cancer: A phase 2 trial

AUTHOR: Burch Patrick A; Croghan Gary A; Gastineau Dennis A; Jones Lori A; Kaur Judith S; Kylstra Jelle W; Richardson Ronald L; Valone Frank H; Vuk-Pavlovic Stanimir (Reprint)

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JOURNAL: Prostate 60 (3): p197-204 August 1, 2004 2004

MEDIUM: print

ISSN: 0270-4137 _(ISSN print)

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: BACKGROUND. Prostate cancer is the most commonly diagnosed malignancy in American men, yet treatment of its metastatic androgen-independent form remains inadequate. This mandates development of new therapies such as immunotherapy. In this Phase 2 trial, we determined the efficacy of antigen presenting cells (APCs) loaded with PA2024, a recombinant fusion protein containing prostatic acid phosphatase (PAP) and GM-CSF. METHODS. We enrolled 21 patients with histologically documented androgen-independent prostate carcinoma that could be evaluated by radionuclide bone scan or computed tomography scan. APC8015 was prepared from a leukapheresis product; it contained autologous CD54-positive PA2024-loaded APCs with admixtures of monocytes, macrophages, B and T cells. APC8015 was infused intravenously twice, 2 weeks apart. Two weeks after the second infusion, patients received three subcutaneous injections of 1.0 mg of PA2024 1 month apart. We monitored patients' physical condition, immune response, and laboratory parameters. RESULTS. Nineteen patients could be evaluated for response to treatment. The median time to progression was 118 days. Treatment was tolerated reasonably well; most adverse effects were secondary to APC8015 and were NCI Common Toxicity Criteria Grade 1-2. Four of the 21 patients reported Grade 3-4 adverse events. Two patients exhibited a transient 25-50% decrease in prostate-specific antigen (PSA). For a third patient, PSA dropped from 221 ng/ml at baseline to undetectable levels by week 24 and has remained so for more than 4 years. In addition, this patient's metastatic retroperitoneal and pelvic adenopathy has resolved. PBMC collected from patients for at least 16 weeks proliferated upon in vitro stimulation by PA2024. For the patient with responsive disease, PBMC could be stimulated for 96 weeks. CONCLUSIONS. This study demonstrates a definite clinical response of androgen-independent prostate cancer to APC immunotherapy. Currently we are studying this mode of therapy in Phase 3 trials. Copyright 2004 Wiley-Liss, Inc.

REGISTRY NUMBERS: 350229-75-3: Provenge; 83869-56-1: granulocyte-macrophage

colony stimulating factor; 9001-77-8: prostatic acid phosphatase
ENZYME COMMISSION NUMBER: EC 3.4.21.77: prostate-specific antigen; EC
3.1.3.2: prostatic acid phosphatase

DESCRIPTORS:

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Clinical
Immunology--Human Medicine, Medical Sciences; Oncology--Human Medicine,
Medical Sciences; Pharmacology

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata,
Animalia

ORGANISMS: human (Hominidae)--male, American

ORGANISMS: PARTS ETC: B cell--blood and lymphatics, immune system; CD54
positive cell--immune system; T cell--blood and lymphatics, immune
system; antigen-presenting cell--immune system, intravenous infusion;
macrophage--blood and lymphatics, immune system; monocyte--blood and
lymphatics, immune system; peripheral blood mononuclear cell {PBMC}--
blood and lymphatics, immune system

COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates;
Vertebrates

DISEASES: androgen-independent prostate cancer--neoplastic disease,
reproductive system disease/male, urologic disease, therapy; metastatic
retroperitoneal adenopathy--disease-miscellaneous; pelvic adenopathy--
disease-miscellaneous; prostate cancer--neoplastic disease,
reproductive system disease/male, urologic disease, diagnosis, therapy

MESH TERMS: Prostatic Neoplasms (MeSH); Prostatic Neoplasms (MeSH)

CHEMICALS & BIOCHEMICALS: PA2024 fusion protein; Provenge {APC8015}--
antineoplastic-drug, immunologic-drug, immunostimulant-drug, phase II
clinical trial; granulocyte-macrophage colony stimulating factor {
GM-CSF}; prostate-specific antigen; prostatic acid phosphatase

METHODS & EQUIPMENT: computed tomography scan--clinical techniques,
diagnostic techniques, imaging and microscopy techniques, laboratory
techniques; immunotherapy--clinical techniques, immunologic techniques
, laboratory techniques, therapeutic and prophylactic techniques;
radionuclide bone scan--clinical techniques, diagnostic techniques

MISCELLANEOUS TERMS: National Cancer Institute {NCI}; National Cancer
Institute common toxicity criteria grade 1-4 {NCI common toxicity
criteria grade 1-4}; immune response

CONCEPT CODES:

02506 Cytology - Animal

02508 Cytology - Human

10060 Biochemistry studies - General

10064 Biochemistry studies - Proteins, peptides and amino acids

12504 Pathology - Diagnostic

12512 Pathology - Therapy

15002 Blood - Blood and lymph studies

15004 Blood - Blood cell studies

15506 Urinary system - Pathology

16506 Reproductive system - Pathology

17002 Endocrine - General

22002 Pharmacology - General

22005 Pharmacology - Clinical pharmacology

22018 Pharmacology - Immunological processes and allergy

24001 Neoplasms - Diagnostic methods

24003 Neoplasms - Immunology

24004 Neoplasms - Pathology, clinical aspects and systemic effects

24008 Neoplasms - Therapeutic agents and therapy

34502 Immunology - General and methods

34508 Immunology - Immunopathology, tissue immunology

BIOSYSTEMATIC CODES:

86215 Hominidae

6/9/10 (Item 3 from file: 5)

DIALOG(R) File 5:Biosis Previews(R)

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0013557956 BIOSIS NO.: 200200151467

Stability characterization of antigen-loaded dendritic cell vaccines

AUTHOR: Nevin Barry (Reprint); Therond Judy; Ishisaka Toshiye (Reprint);

Shiomoto Clifford; Kothari Sudesh S (Reprint); Galie Brian; Yumiaco

Orlando Jr; Westerman Rick; Terral Annette; Peshwa Madhusudan V (Reprint)

AUTHOR ADDRESS: Cell Process Development, Dendreon, Seattle, WA, USA**USA

JOURNAL: Blood 98 (11 Part 2): p38b November 16, 2001 2001

MEDIUM: print

CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of

Hematology, Part 2 Orlando, Florida, USA December 07-11, 2001; 20011207

SPONSOR: American Society of Hematology

ISSN: 0006-4971

DOCUMENT TYPE: Meeting; Meeting Abstract

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Provenge™, an immunotherapy product consisting of autologous dendritic cells (DC) loaded ex vivo with a recombinant engineered prostate tumor-antigen (PA2024) consisting of prostatic acid phosphatase (PAP) fused to granulocyte macrophage colony stimulating factor (GM-CSF), is currently in phase III clinical evaluation for treatment of hormone refractory prostate cancer. The patients leukapheresis product was shipped to Dendreon's cGMP cell processing centers where it was processed to enrich dendritic cells, incubated with PA2024 for 36-44 hours, then harvested and formulated in Lactated Ringer's solution for injection, USP and returned to the clinical site for administration. Stability studies were designed wherein the final DC vaccine product was stored refrigerated at 2-8degreeC and samples were analyzed at 0, 8, 12, 24, 30 and 36 hours post-formulation. Samples were characterized for nucleated cell number, cell viability, phenotype, potency, and allogeneic and autologous T cell stimulatory capacity. The dendritic cell fraction was characterized for expression of a variety of co-stimulatory molecules including CD1a, CD11c, CD40, CD54, CD80, CD83, CD86, CD123, HLA-DR, and HLA-A,B,C. Results indicate that there is no difference in any of the product characteristics between 0 and 8 hours. Beyond 8 hours there was no difference in cell viability and phenotype over the stability period evaluated. There was approximately a 10-20% decrease in cell number, potency and T cell stimulatory capacity over a course of 36 hours. The implications of the observed in vitro results on in vivo potency will be discussed.

REGISTRY NUMBERS: 350229-75-3: Provenge; 83869-56-1: granulocyte macrophage colony stimulating factor

DESCRIPTORS:

MAJOR CONCEPTS: Clinical Immunology--Human Medicine, Medical Sciences;

Oncology--Human Medicine, Medical Sciences; Pharmacology

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGANISMS: human (Hominidae)--patient

ORGANISMS: PARTS ETC: T cell--blood and lymphatics, immune system; dendritic cells--immune system

COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates

DISEASES: prostate cancer--neoplastic disease, reproductive system disease/male, urologic disease

MESH TERMS: Prostatic Neoplasms (MeSH)
 CHEMICALS & BIOCHEMICALS: Provenge--antineoplastic-drug,
 immunologic-drug, stability, vaccine; granulocyte macrophage colony
 stimulating factor; prostate tumor-antigen; prostatic acid phosphatase
 MISCELLANEOUS TERMS: Meeting Abstract; Meeting Abstract
 CONCEPT CODES:
 00520 General biology - Symposia, transactions and proceedings
 02506 Cytology - Animal
 02508 Cytology - Human
 12512 Pathology - Therapy
 15002 Blood - Blood and lymph studies
 15004 Blood - Blood cell studies
 15506 Urinary system - Pathology
 16506 Reproductive system - Pathology
 22002 Pharmacology - General
 22005 Pharmacology - Clinical pharmacology
 22018 Pharmacology - Immunological processes and allergy
 24003 Neoplasms - Immunology
 24004 Neoplasms - Pathology, clinical aspects and systemic effects
 24008 Neoplasms - Therapeutic agents and therapy
 34502 Immunology - General and methods
 34508 Immunology - Immunopathology, tissue immunology
 BIOSYSTEMATIC CODES:
 86215 Hominidae

6/9/11 (Item 1 from file: 73)
 DIALOG(R)File 73:EMBASE
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13316952 EMBASE No: 2005387607
Session II: Tumor antigens - Prostate cancer antigens and vaccines
 Salgaller M.L.; Elgamal A.-A.; Bosch M.; Lodge A.; Shankar G.; Boynton A.
 ; Belldegrun A.; Logothetis C.; Papandreou C.
 Dr. M.L. Salgaller, Northwest Biotherapeutics, Inc., Seattle, WA United
 States
 Cancer Immunology, Immunotherapy (CANCER IMMUNOL. IMMUNOTHER.) (Germany
) 2003, 52/SUPPL. 1 (S8-S9+S27)
 CODEN: CIIMD ISSN: 0340-7004
 DOCUMENT TYPE: Journal ; Conference Paper
 LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The clinical development of prostate cancer vaccines presents several challenges. Reagents are more limited and difficult to obtain as compared with other tumor types. The advanced age of the patient population presents the researcher with subjects having diminished immune systems and who are often less willing to undergo procedures for research purposes. Consequently, the majority of research has involved those cancers for which tumor and immune cells are readily available. Despite these hurdles, new and novel approaches are improving the poor overall survival rates through the development of antigen-based treatment options. These efforts are particularly important in the realm of hormone-refractory prostate cancer (HRPC), since no therapy exists with significant clinical impact. This is a major issue for the 36,000 men who will die from the disease annually, despite transient responses to secondary treatment such as hormone ablation therapy. During the past few years, candidate target antigens for experimental vaccines have been identified in several laboratories. These include oncogenes, overexpressed proteins, and carbohydrates. Three of the furthest in clinical development are well-established clinical markers of prostate cancer: prostate-specific membrane antigen (PSMA),

prostate-specific antigen (PSA), and prostatic acid phosphatase (PAP). Following conclusive preclinical evidence indicating that the human body responds immunologically to prostate antigens, clinical trials have been underway for many years with PSMA, PSA, and PAP as targets. We investigated the capacity of a vaccine composed of autologous dendritic cells (DC), pulsed ex vivo with recombinant PSMA (rPS-MA), to safely generate clinically meaningful antitumor immune responses in HRPC patients. In 2000 and 2001, 32 patients with metastatic or non-metastatic HRPC were enrolled in a phase I/II clinical trial. Their peripheral blood mononuclear cells were isolated by leukapheresis, matured to DC by in vitro culture with maturation factors (GM-CSF, IL-4, and inactivated BCG) for up to 7 days, followed by rPSMA loading and harvesting of the vaccine. Patients received four intradermal treatments of 5, 10, or 20-million rPSMA-loaded mature DC at monthly intervals, followed by up to a total of 6 months of observation. Measurement of serum anti-PSMA antibodies, PSMA-stimulated lymphocyte proliferation, and delayed-type hypersensitivity (DTH) skin testing were carried out before, during, and after vaccination. Clinical responses were assessed by CT/bone scans and hematochemical laboratory tests, including PSA levels. More than 140 total vaccine injections were well tolerated; no clinical signs of autoimmunity or serious adverse events were observed. Overall, 54% of patients achieved stability of their disease at >6 months follow-up, as assessed by radiographic criteria, and 83% of patients had a PSMA-specific immune response, 92% of patients with stable disease had a PSMA-specific immune response, and 46% of patients had a decrease in PSA velocity. Compared to baseline, 93% of 27 evaluable patients converted to DTH-positive against the BCG component of the vaccine. Due to these promising initial findings we have initiated a double-blind, placebo-controlled phase III clinical trial. (c) 2002 Northwest Biotherapeutics, Inc. All rights reserved.

DRUG DESCRIPTORS:

*tumor antigen; *cancer vaccine--adverse drug reaction--ae; *cancer vaccine--clinical trial--ct; *cancer vaccine--drug therapy--dt
 tumor rejection antigen; tumor suppressor protein; prostate antigen; acid phosphatase prostate isoenzyme; prostate specific antigen; prostate specific membrane antigen--drug therapy--dt; prostate specific membrane antigen--intradermal drug administration--dl; prostate specific membrane antigen--pharmacology--pd; recombinant antigen--drug therapy--dt; recombinant antigen--intradermal drug administration--dl; recombinant antigen--pharmacology--pd; dendritic cell vaccine--adverse drug reaction--ae; dendritic cell vaccine--clinical trial--ct; dendritic cell vaccine--drug therapy--dt

MEDICAL DESCRIPTORS:

*prostate cancer--drug therapy--dt
 prostatectomy; cancer surgery; bone metastasis; cancer cell culture; T lymphocyte; medical research; cancer chemotherapy; immune response; cancer survival; quality of life; dendritic cell; peripheral blood mononuclear cell; skin irritation--side effect--si; injection site reaction--side effect--si; headache--side effect--si; fatigue--side effect--si; human; clinical trial; conference paper; priority journal

SECTION HEADINGS:

- 016 Cancer
- 026 Immunology, Serology and Transplantation
- 028 Urology and Nephrology
- 037 Drug Literature Index
- 038 Adverse Reaction Titles

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07378239 EMBASE No: 1998268893

Defective expression of granulocyte-macrophage colony-stimulating factor/interleukin-3/interleukin-5 receptor common beta chain in children with acute myeloid leukemia associated with respiratory failure

Dirksen U.; Hattenhorst U.; Schneider P.; Schroten H.; Gobel U.; Bocking A.; Muller K.-M.; Murray R.; Burdach S.

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Blood (BLOOD) (United States) 15 AUG 1998, 92/4 (1097-1103)

CODEN: BLOOA ISSN: 0006-4971

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 35

Deficiency of the granulocyte-macrophage colony-stimulating factor (GM-CSF)/interleukin-3 (IL-3)/IL-5 receptors common beta chain (betac) is a cause of fatal respiratory failure. betac deficiency manifests as pulmonary alveolar proteinosis (PAP). PAP has heterogenous etiologies that may be genetic or aquired. Some cases of PAP have been reported to be associated with hematologic malignancies such as acute myeloid leukemia (AML). in mice, the PAP phenotype was generated by targeted deletion of the gene for betac and can be treated by transplantation of wild-type bone marrow into betac -/- mice. Thus, our findings in betac -/- mice provide evidence for a causal relationship between the lung disease and the hematopoietic system. We describe here expression defects of betac or betac plus GM-CSF receptor alpha chain (GM-CSFR alpha) in 3 pediatric patients with AML and PAP symptoms. All of the patients' leukemic cells failed to express normal levels of betac. The leukemic cells of patients no. 2 and 3 additionally lacked the expression of GM-CSFR alpha, as shown by flow cytometry. Strikingly reduced or absent function of betac was demonstrated in clonogenic progenitor assays with absent colony-forming unit (CFU) growth after GM-CSF or IL-3 stimulation. The response to growth factors acting via a growth factor receptor distinct from the GM-CSF/IL-3/IL-5 system (recombinant human granulocyte colony-stimulating factor [rhG-CSF]) was normal. After antileukemic treatment, the pulmonary symptoms resolved and betac or betac plus GM-CSFR alpha expression was normal. Our findings provide evidence that a defect in the expression of betac or betac plus GM-CSFR alpha on AML blasts can be associated with respiratory failure in patients with AML.

DRUG DESCRIPTORS:

*granulocyte macrophage colony stimulating factor receptor--endogenous compound--ec; *interleukin 3 receptor--endogenous compound--ec; *interleukin 5 receptor--endogenous compound--ec
interleukin 3; interleukin 5; recombinant granulocyte colony stimulating factor; apolipoprotein a--endogenous compound--ec; apolipoprotein b
--endogenous compound--ec; antileukemic agent

MEDICAL DESCRIPTORS:

*acute granulocytic leukemia--diagnosis--di; *acute granulocytic leukemia--etiology--et; *acute granulocytic leukemia--radiotherapy--rt; *acute granulocytic leukemia--surgery--su; *respiratory failure--complication--co; *respiratory failure--diagnosis--di; *respiratory failure--etiology--et; *lung alveolus proteinosis--complication--co; *lung alveolus proteinosis--diagnosis--di; *lung alveolus proteinosis--etiology--et
protein expression; flow cytometry; clonogenic assay; colony forming unit; thorax radiography; lung lavage; mononuclear cell; allogenic bone marrow transplantation; cancer chemotherapy; whole body radiation; human; male;

female; case report; controlled study; human cell; infant; school child;
article; priority journal
CAS REGISTRY NO.: 121181-53-1 (recombinant granulocyte colony stimulating
factor)

SECTION HEADINGS:

005 General Pathology and Pathological Anatomy
015 Chest Diseases, Thoracic Surgery and Tuberculosis
025 Hematology
029 Clinical and Experimental Biochemistry

6/9/13 (Item 3 from file: 73)

DIALOG(R)File 73:EMBASE

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06852713 EMBASE No: 1997135313

**Effects of Phytolacca acinosa polysaccharides I with different schedules
on its antitumor efficiency in tumor bearing mice and production of IL-1,
IL-2, IL-6, TNF, CSF activity in normal mice**

Wang H.-B.; Zheng Q.-W.

H.-B. Wang, Department of Pharmacology, College of Pharmacy, Second
Military Medical University, Shanghai 200433 China

Immunopharmacology and Immunotoxicology (IMMUNOPHARMACOL. IMMUNOTOXICOL.
) (United States) 1997, 19/2 (197-213)

CODEN: IITOE ISSN: 0892-3973

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 29

Effects of Phytolacca acinosa polysaccharides I (PAP-I), 5-40 mg/kg in
timing of 7 times/wk, 3 times/wk and 1 time/wk on their antitumor
efficiency in Sarcoma-180 bearing mice were comparatively investigated. The
results confirmed that PAP-I (10 mg/kg, 3 times/wk) reached its optimal
antitumor efficiency. Concanavalin A-, lipopolysaccharides-induced
lymphocyte proliferation and the IL-2 production were tested in normal mice
which were treated with PAP-I, 5-50 mg/kg in timing of 1 time/wk and 3
times/wk. The results showed that PAP-I could augment lymphocyte
proliferation and IL-2 production in the group treated with PAP-I in timing
of once a week. However, in the group 3 times/wk, PAP-I could significantly
weaken lymphocyte proliferation and IL-2 production. Further studies on
IL-1, TNF and IL-6 secreted from macrophages and the level of CSF activity
in serum of normal mice with different schedules showed that PAP-I (10
mg/kg, 3 times/wk) was the best one in regulating the production of IL-1,
TNF, IL-6 and CSF activity. M-CSF was confirmed in the serum by using
monoclonal antibody of IL-3, GM-CSF and polyclonal antibody of M-CSF. These
results suggested that the antitumor effect of PAP-I, may be mainly related
to its augmenting effect on macrophages in mice.

DRUG DESCRIPTORS:

*interleukin 1--endogenous compound--ec; *interleukin 2--endogenous
compound--ec; *interleukin 6--endogenous compound--ec; *plant extract
--pharmacology--pd; *plant extract--drug dose--do; *polysaccharide
--pharmacology--pd; *polysaccharide--drug dose--do; *tumor necrosis factor
--endogenous compound--ec

MEDICAL DESCRIPTORS:

*antineoplastic activity; *macrophage
animal cell; article; intraperitoneal drug administration; mouse; nonhuman;
priority journal

CAS REGISTRY NO.: 85898-30-2 (interleukin 2)

SECTION HEADINGS:

016 Cancer
 026 Immunology, Serology and Transplantation
 030 Clinical and Experimental Pharmacology
 037 Drug Literature Index

6/9/14 (Item 1 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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14931093 Genuine Article#: 021CY Number of References: 50

Title: Aerosol granulocyte-macrophage colony-stimulating factor for pulmonary alveolar proteinosis

Author(s): Wylam ME (REPRINT) ; Ten R; Prakash UBS; Nadrous HF; Clawson ML; Anderson PM

Corporate Source: Mayo Clin,Coll Med, Dept Internal Med & Paediat,200 1st St,SW/Rochester//MN/55905 (REPRINT); Mayo Clin,Coll Med, Dept Internal Med & Paediat,Rochester//MN/55905(wylam.mark@mayo.edu)

Journal: EUROPEAN RESPIRATORY JOURNAL, 2006, V27, N3 (MAR), P585-593

ISSN: 0903-1936 **Publication date:** 20060300

Publisher: EUROPEAN RESPIRATORY SOC JOURNALS LTD, 146 WEST ST, STE 2.4, HUTTONS BLDG, SHEFFIELD S1 4ES, ENGLAND

Language: English **Document Type:** ARTICLE

Geographic Location: USA

Journal Subject Category: RESPIRATORY SYSTEM

Abstract: Recently, granulocyte-macrophage colony-stimulating factor (GM-CSF) autoantibodies have been found in many patients with pulmonary alveolar proteinosis (PAP). The present study reports a retrospective case series of patients who used aerosolised GM-CSF in the treatment of idiopathic PAP. Between 1999 and 2003, 12 patients elected to receive aerosolised GM-CSF (250 fig b.i.d. every other week) in lieu of whole-lung lavage or observation.

Patient characteristics, pulmonary function tests, arterial blood gas analysis, laboratory values and chest radiographs were extracted from the patient's medical records. Of the six patients tested, all had GM-CSF neutralising antibodies. Additionally, abnormalities in GM-CSF gene expression (one patient), receptor expression (two patients) and ability to upregulate adhesion molecules (one patient) were found.

All patients except one had a positive response (mean improvements in arterial oxygen tension, alveolar-arterial oxygen gradient, carbon monoxide diffusing capacity of the lung and forced vital capacity were 17.1 mmHg, 18.4 mmHg, 16.6% pred and 13.5% pred, respectively). Two patients made a complete recovery and were disease free 1 and 2 yrs after discontinuing treatment. Four patients showed complete response to both the initial course or when treated again for recurrence after discontinuation of treatment. One patient required dose escalation (500 jig b.i.d.) with complete response. GM-CSF was well tolerated without late toxicity after median (range) follow-up of 30.5 (3-68) months.

In conclusion, aerosolised granulocyte-macrophage colony-stimulating factor is safe and effective in treating pulmonary alveolar proteinosis providing an alternative to whole-lung lavage or subcutaneous granulocyte-macrophage colony-stimulating factor.

Descriptors--Author Keywords: granulocyte-macrophage colony-stimulating factor ; pulmonary alveolar proteinosis ; surfactant

Identifiers--KeyWord Plus(R): FACTOR-DEFICIENT MICE; GM-CSF THERAPY; CANCER-PATIENTS; FACTOR-RECEPTOR; LUNG LAVAGE; EXPRESSION; DISEASE; AUTOANTIBODIES; HOMEOSTASIS; PATHOLOGY

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11263714 Genuine Article#: 631VN Number of References: 31

Title: Anti-GM-CSF titer predicts response to GM-CSF therapy in pulmonary alveolar proteinosis

Author(s): Bonfield TL (REPRINT) ; Kavuru MS; Thomassen MJ

Corporate Source: Cleveland Clin Fdn, Dept Pulm & Crit Care Med, 9500 Euclid Ave/Cleveland//OH/44195 (REPRINT); Cleveland Clin Fdn, Dept Pulm & Crit Care Med, Cleveland//OH/44195; Cleveland Clin Fdn, Dept Cell Biol, Cleveland//OH/44195

Journal: CLINICAL IMMUNOLOGY, 2002, V105, N3 (DEC), P342-350

ISSN: 1521-6616 Publication date: 20021200

Publisher: ACADEMIC PRESS INC ELSEVIER SCIENCE, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA

Language: English Document Type: ARTICLE

Geographic Location: USA

Journal Subject Category: IMMUNOLOGY

Abstract: Pulmonary alveolar proteinosis (PAP) is an idiopathic disease characterized by the accumulation of surfactant in the pulmonary airspaces. The development of a PAP-like syndrome in the GM-CSF knockout mouse and resolution of disease by local GM-CSF expression strongly implicates GM-CSF in surfactant; homeostasis and disease pathogenesis. Based on murine data, GM-CSF therapy was administered to PAP patients, with a subset of response to GM-CSF therapy in some patients is unexplained. In adult idiopathic PAP there appears to be no intrinsic cellular defect in synthesizing or secreting GM-CSF and/or function in the GM-CSF receptor. Subsequent studies have shown the presence of circulating, neutralizing anti-GM-CSF antibodies in all adult PAP patients studied to date. Whether the anti-GM-CSF is causally related to the PAP disease and whether it should be the target of manipulation remains to be determined. The present study quantified the anti-GM-CSF levels sequentially in PAP patients receiving GM-CSF therapy. The data indicate that titers of circulating anti-GM-CSF predict response to GM-CSF therapy. In addition, we present data from a patient undergoing plasma exchange in which anti-GM-CSF titer decreased with improvement. These data support the hypothesis that PAP is an anti-GM-CSF autoimmune disease due to the development of antibodies, which results in the deactivation or neutralization of GM-CSF. (C) 2002 Elsevier Science (USA).

Identifiers--KeyWord Plus(R): COLONY-STIMULATING FACTOR; FACTOR-DEFICIENT MICE; BETA-2 RECEPTOR; PATHOLOGY; DISEASE; CANCER; VALUES; DEFECT

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6/9/16 (Item 3 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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10089054 Genuine Article#: 484GB Number of References: 26

Title: Change in cytokeratin 19 fragment level according to the severity of pulmonary alveolar proteinosis

Author(s): Minakata Y (REPRINT) ; Kida Y; Nakanishi H; Nishimoto T; Yukawa S

Corporate Source: Wakayama Med Univ, Dept Internal Med 3, Sch Med, 811-1
 Kimiidera/Wakayama 6410012//Japan/ (REPRINT); Wakayama Med Univ, Dept
 Internal Med 3, Sch Med, Wakayama 6410012//Japan/

Journal: INTERNAL MEDICINE, 2001, V40, N10 (OCT), P1024-1027

ISSN: 0918-2918 Publication date: 20011000

Publisher: JAPAN SOC INTERNAL MEDICINE, 34-3 3-CHOME HONGO BUNKYO-KU,
 TOKYO, 113, JAPAN

Language: English Document Type: ARTICLE

Geographic Location: Japan

Journal Subject Category: MEDICINE, GENERAL & INTERNAL

Abstract: A 48-year-old man was diagnosed with primary alveolar proteinosis (PAP). Whole lung lavage was performed for treatment, and the opacity on his chest X-ray completely disappeared. The value of cytokeratin 19 fragment (CYFRA) in the serum was high at the beginning, decreased after lung lavage, and became elevated again when the disease recurred 7 months later. As PAP is thought to be a problem of surfactant secreted from type II pneumocytes, and a cytokeratin is present in the alveolar epithelial tissue, the value of serum CYFRA might be related to the severity of PAP.

Descriptors--Author Keywords: GM-CSF ; CYFRA ; alveolar type II cell

Identifiers--KeyWord Plus(R): COLONY-STIMULATING FACTOR; LUNG-CANCER;
 CARCINOEMBRYONIC ANTIGEN; DEFICIENT MICE; PATHOLOGY; SERUM; ELEVATION;
 MARKERS; ASSAY

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6/9/17 (Item 4 from file: 34)

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07147994 Genuine Article#: 128AZ Number of References: 61

Title: Attenuated hematopoietic response to granulocyte-macrophage colony-stimulating factor in patients with acquired pulmonary alveolar proteinosis

Author(s): Seymour JF (REPRINT) ; Begley CG; Dirksen U; Presneill JJ;
 Nicola NA; Moore PE; Schoch OD; vanAsperen P; Roth B; Burdach S; Dunn AR

Corporate Source: PETER MACCALLUM CANC INST, LOCKED BAG 1, A BECKETT
 ST/MELBOURNE/VIC 3000/AUSTRALIA/ (REPRINT); LUDWIG INST CANC
 RES,/PARKVILLE/VIC/AUSTRALIA/; ROTARY BONE MARROW RES
 LABS,/PARKVILLE/VIC/AUSTRALIA/; UNIV DUSSELDORF, MED CTR, DEPT PEDIAT
 HEMATOL ONCOL/D-4000 DUSSELDORF//GERMANY/; ROYAL MELBOURNE HOSP, DEPT
 CLIN HAEMATOL & MED ONCOL/PARKVILLE/VIC 3050/AUSTRALIA/; ROYAL
 MELBOURNE HOSP, INTENS CARE UNIT/PARKVILLE/VIC 3050/AUSTRALIA/; WALTER &
 ELIZA HALL INST MED RES,/PARKVILLE/VIC/AUSTRALIA/; CHILDRENS HOSP, DIV
 RESP MED/BOSTON//MA/; UNIV ZURICH HOSP, DIV PULM/CH-8091
 ZURICH//SWITZERLAND/; ROYAL ALEXANDRA HOSP
 CHILDREN,/WESTMEAD/NSW/AUSTRALIA/; UNIV COLOGNE, DEPT
 PEDIAT/COLOGNE//GERMANY/

Journal: BLOOD, 1998, V92, N8 (OCT 15), P2657-2667

ISSN: 0006-4971 Publication date: 19981015

Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE
 300, PHILADELPHIA, PA 19106-3399

Language: English Document Type: ARTICLE

Geographic Location: AUSTRALIA; GERMANY; USA; SWITZERLAND

Subfile: CC LIFE--Current Contents, Life Sciences; CC CLIN--Current
 Contents, Clinical Medicine

Journal Subject Category: HEMATOLOGY

Abstract: The pathogenesis of acquired pulmonary alveolar proteinosis (PAP), a rare lung disease characterized by excessive surfactant accumulation within the alveolar space, remains obscure. Gene-targeted mice lacking the hematopoietic growth factor granulocyte-macrophage colony-stimulating factor (GM-CSF) or the signal-transducing beta-common chain of the GM-CSF receptor have impaired surfactant clearance and pulmonary pathology resembling human PAP. We therefore investigated the hematopoietic effects of GM-CSF in patients with PAP. The hematologic response of 5 infants with congenital PAP to 5 mu g/kg/d was of normal magnitude. By contrast, despite normal expression of GM-CSF receptor alpha- and beta-common chains on peripheral blood myelomonocytic cells (n = 6) and normal binding affinity of bone marrow mononuclear cells for GM-CSF (n = 3), each of the 12 patients with acquired PAP treated displayed impaired responses to GM-CSF; 5 mu g/kg/d produced only minor eosinophilia, and doses of 7.5 to 20 mu g/kg were required to induce greater than or equal to 1.5-fold neutrophil increments in the 3 patients who underwent dose-escalation. However,

neutrophilic responses to 5 μ g/kg granulocyte colony-stimulating factor (G-CSF) were normal ($n = 4$). In vitro, the proportion of hematopoietic progenitors responsive to GM-CSF (16.1% \pm 8.9%; $P = .042$) or interleukin-3 (IL-3: 19.3% \pm 7.7%; $P = .063$), both of which utilize the beta-common chain of the GM-CSF receptor complex, were reduced among patients with acquired PAP ($n = 4$) compared with normal bone marrow donor controls (47.2% \pm 25.9% and 40.9% \pm 18.6%, respectively). In the one individual who had complete resolution of lung disease during the period of study, this was temporally associated with correction of this defective in vitro response to GM-CSF and IL-3 on serial assessment. These data establish that patients with acquired PAP have an associated impaired responsiveness to GM-CSF that is potentially pathogenic in the development of their lung disease. Based on these observations, we propose a model of the pathogenesis of acquired PAP that suggests the disease arises as a consequence of an acquired clonal disorder within the hematopoietic progenitor cell compartment. (C) 1998 by The American Society of Hematology.

Identifiers--Keyword Plus(R): RECEPTOR-DEFICIENT MICE; COMMON BETA-CHAIN; FACTOR GM-CSF; ADVANCED MALIGNANCY; PROGENITOR CELLS; GENE-EXPRESSION; STEM-CELLS; IN-VITRO; PHASE-I; CANCER

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6/9/18 (Item 5 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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03729247 Genuine Article#: QA899 Number of References: 16

Title: A NOVEL, SIMPLE, RELIABLE, AND SENSITIVE METHOD FOR MULTIPLE
IMMUNOENZYME STAINING - USE OF MICROWAVE-OVEN HEATING TO BLOCK ANTIBODY
CROSS-REACTIVITY AND RETRIEVE ANTIGENS

Author(s): LAN HY; MU W; NIKOLICPATERSON DJ; ATKINS RC

Corporate Source: MONASH MED CTR,DEPT NEPHROL,246 CLAYTON RD/CLAYTON/VIC
3168/AUSTRALIA/

Journal: JOURNAL OF HISTOCHEMISTRY & CYTOCHEMISTRY, 1995, V43, N1 (JAN), P
97-102

ISSN: 0022-1554

Language: ENGLISH Document Type: NOTE

Geographic Location: AUSTRALIA

Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences

Journal Subject Category: CELL BIOLOGY

Abstract: We report a simple and reliable method for detection of two or more antigens within tissue sections by indirect immunoenzyme staining using mouse monoclonal antibodies (MAbs). This technique involves treating sections with two 5-min microwave (MW) oven heatings between sequential rounds of three-layer immunoenzyme staining (mouse MAb, goat anti-mouse IgG, and mouse PAP or mouse APAAP) and color development. Discrete staining of cell surface, cytoplasmic, and nuclear antigens was evident within individual cells. This technique has a number of advantages over those currently available. First, MW treatment denatures bound antibody molecules, thereby completely blocking crossreactivity between sequential rounds of staining. This allows the use of primary (and other) antibodies raised in the same species and the use of a sensitive three-layer staining method. Second, antigen retrieval after MW treatment markedly increases the sensitivity of cytoplasmic and nuclear antigen detection. Third, inactivation of peroxidase and alkaline phosphatase enzymes present in PAP and APAAP complexes prevents inappropriate color development. Finally, this method can be used in both paraformaldehyde-fixed cryostat sections and

formalin-fixed paraffin tissue sections. In conclusion, this is a simple, reliable, and sensitive technique that will be useful in many areas of diagnosis and research.

Descriptors--Author Keywords: MULTIPLE IMMUNOENZYME STAINING ; MICROWAVE ; ANTIBODY DENATURATION ; ANTIGEN RETRIEVAL ; LEUKOCYTE ; PROLIFERATION

Identifiers--KeyWords Plus: MONOCLONAL-ANTIBODIES; TISSUE-SECTIONS; RECEPTOR

Research Fronts: 93-2411 001 (RAT MICROGLIAL CELLS; CYTOKINE EXPRESSION OF MACROPHAGES; CULTURED ASTROCYTES; AUTOIMMUNE POTENTIAL; NEUROLOGICAL DISEASE; DIFFERENTIAL INDUCTION)

93-2612 001 (MALIGNANT FIBROUS HISTIOCYTOMA; GIANT-CELL TUMORS; PRIMARY RHABDOMYOSARCOMA; MACROPHAGE IMMUNOPHENOTYPE; CLINICOPATHOLOGICAL FEATURES; GM-CSF M-CSF)

93-3155 001 (PROLIFERATING CELL NUCLEAR ANTIGEN; PROGNOSTIC IMPACT IN ARCHIVAL PARAFFIN-EMBEDDED NODE-NEGATIVE BREAST-CANCER; IMMUNOHISTOCHEMICAL EVIDENCE)

93-3816 001 (KI-67 ANTIGEN; P53-PROTEIN EXPRESSION; FIXED PROLIFERATING CELLS; IMMUNOHISTOLOGICAL DETECTION; MICROWAVES IN IMMUNOHISTOCHEMICAL TECHNIQUES)

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